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FILE COVERS 1907 - 21 Nov 2005 VOL 143 ISS 22

FILE LAST UPDATED: 20 Nov 2005 (20051120/ED)

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L11 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:216909 HCAPLUS

DN 142:291401

TI Use of agents that reduce the effect of prokineticin 1 on a prokineticin receptor for the treatment of menorrhagia, dysmenorrhea or endometriosis

IN Jabbour, Henry Nicolas; Millar, Robert Peter

PA Ardana Bioscience Limited, UK

SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005021750	A1	20050310	WO 2004-GB3600	20040824
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI GB 2003-20238 A 20030829

AB A method of combating menorrhagia, dysmenorrhea or endometriosis in a female individual is disclosed, the method comprising administering to the individual at least one agent that reduces the effect of prokineticin 1 on a prokineticin receptor.

IT 144743-92-0, Teverelix

RL: DEV (Device component use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(agents that reduce effect of prokineticin 1 on prokineticin receptor for treatment of menorrhagia, dysmenorrhea or endometriosis)

IT 144743-92-0, Teverelix

RL: DEV (Device component use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

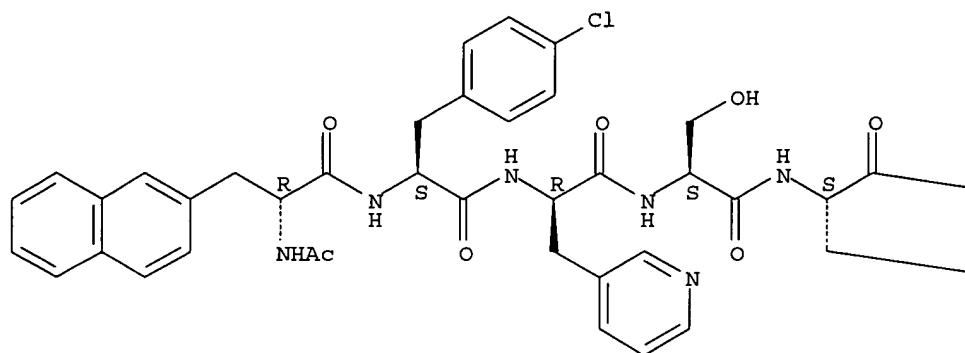
(agents that reduce effect of prokineticin 1 on prokineticin receptor
for treatment of menorrhagia, dysmenorrhea or endometriosis)

RN 144743-92-0 HCAPLUS

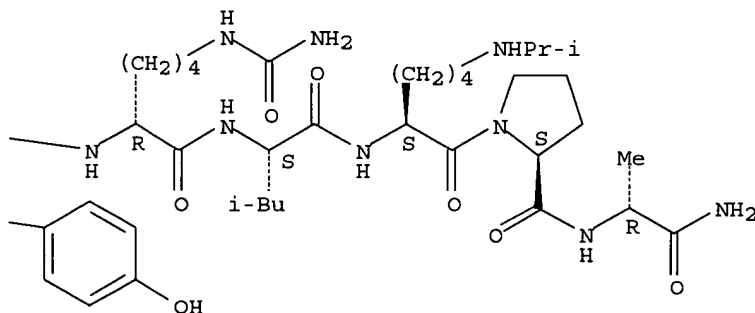
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:964606 HCAPLUS
DN 141:400934
TI Implants for non-radioactive brachytherapy of hormonal-insensitive cancers
IN Deghenghi, Romano
PA Switz.
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004224000	A1	20041111	US 2003-430132	20030505
	WO 2004098560	A1	20041118	WO 2004-EP4672	20040503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-430132 A 20030505

AB Implants are described for use in a novel therapy of hormone-insensitive tumors. The implants are inserted near, around or inside such tumors to provide a high local concentration and sustained release of a gonadotropin-releasing hormone agonist or antagonist and a direct inhibitory action on the growth of such tumors. As the implants are not radioactive, the deleterious side-effects of radioactive treatments are avoided.

IT 144743-92-0, Teverelix

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (GRH antagonist; implants for non-radioactive brachytherapy of hormonal-insensitive cancers)

IT 144743-92-0, Teverelix

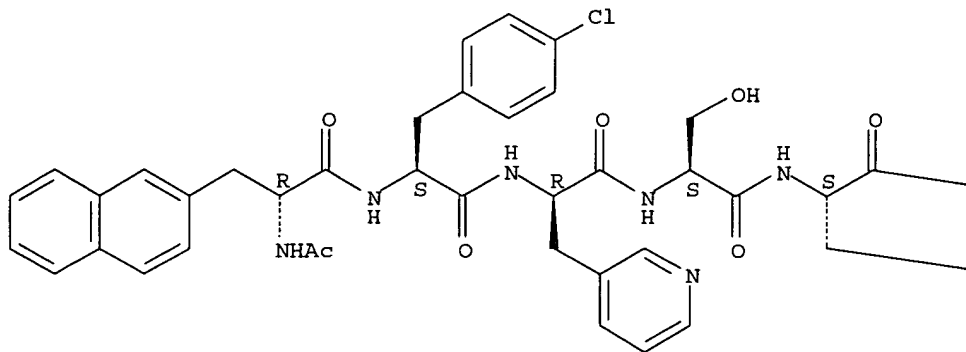
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (GRH antagonist; implants for non-radioactive brachytherapy of hormonal-insensitive cancers)

RN 144743-92-0 HCAPLUS

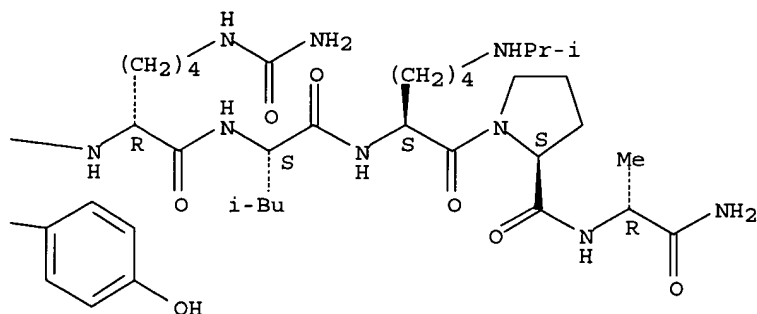
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:857446 HCAPLUS

DN 141:326194

TI Gonadotropin releasing hormone (GnRH) analogs conjugates with steroid hormones and therapeutic uses thereof

IN Millar, Robert Peter

PA Ardana Bioscience Limited, UK

SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004087215	A1	20041014	WO 2004-GB1478	20040405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI GB 2003-7777 A 20030404

AB A compound comprising a gonadotrophin releasing hormone analog conjugated to a hormone moiety, or a derivative thereof, which is able to bind to a plasma hormone binding protein. The compds. may be used to treat hormone-dependent disorders such as cancer, or as a contraceptive.

IT 144743-92-0, Teverelix

RL: RCT (Reactant); RACT (Reactant or reagent)
 (gonadotropin releasing hormone (GnRH) analogs conjugates with steroid hormones and therapeutic uses thereof)

IT 144743-92-0, Teverelix

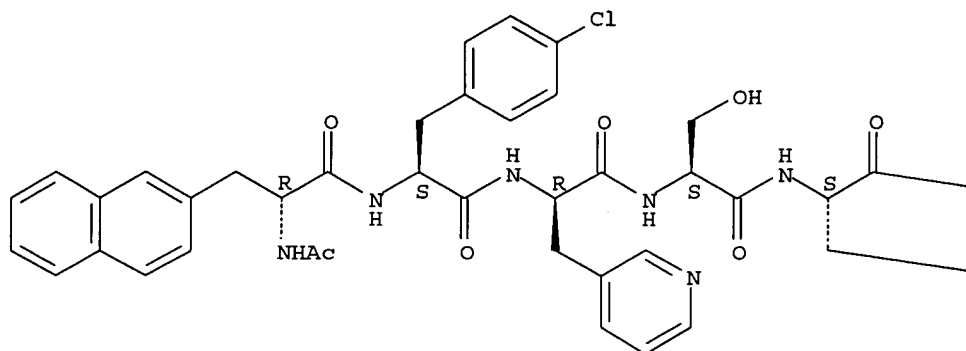
RL: RCT (Reactant); RACT (Reactant or reagent)
 (gonadotropin releasing hormone (GnRH) analogs conjugates with steroid hormones and therapeutic uses thereof)

RN 144743-92-0 HCAPLUS

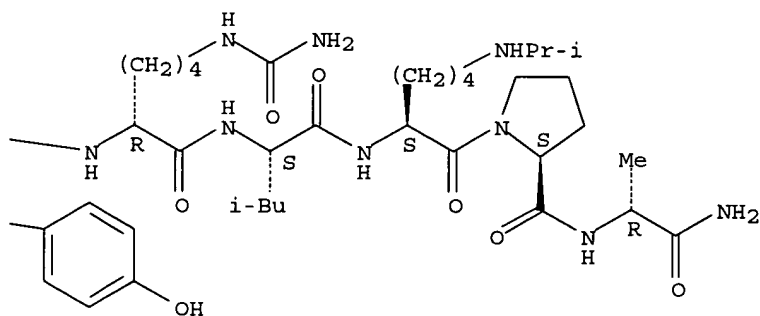
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:756616 HCAPLUS
DN 141:248811
TI New process for the production of pharmaceutical implants
IN Deghenghi, Romano
PA Ardana Bioscience Limited, UK
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078160	A1	20040916	WO 2004-GB816	20040301
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,				

GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2003-4726 A 20030301

AB There is provided a process for the preparation of an implantable or an injectable pharmaceutical composition suitable for the extended release of an active ingredient, such as a peptide or a peptide analog, to a patient following administration, which process comprises: (a) wet granulation of a mixture of active ingredient and PLGA; (b) drying the granules so formed; (c) grinding the dried granules; and (d) extruding the ground product of step (c). Implants comprising 22.5 mg leuporelin were cut from the drug-PLGA extrudates. Each implant weighed 90 mg and included 23.6-26.2 mg leuporelin acetate.

IT 144743-92-0, Teverelix

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(process for production of implants)

IT 144743-92-0, Teverelix

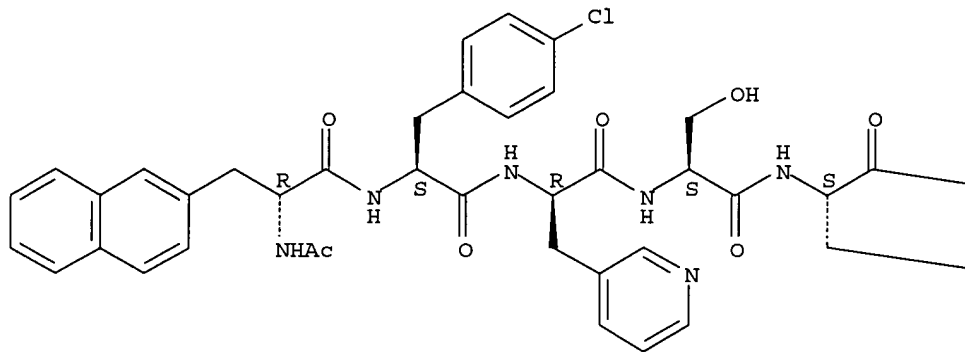
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(process for production of implants)

RN 144743-92-0 HCAPLUS

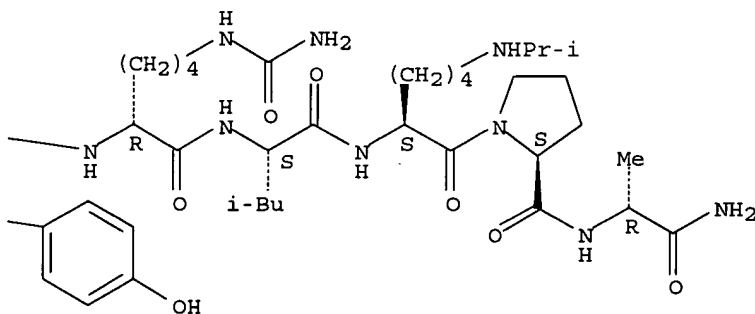
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



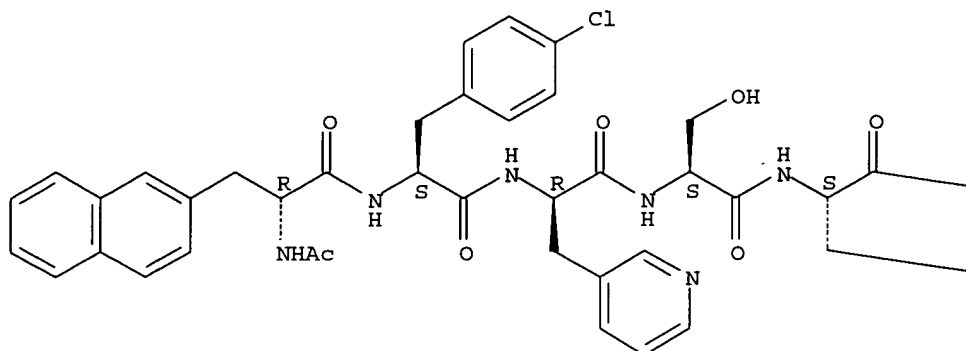
RE.CNT 2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

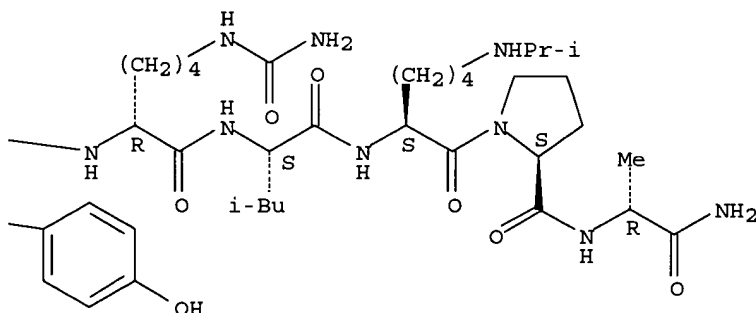
L11 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:856988 HCAPLUS
 DN 140:139750
 TI Suppression and recovery of LH secretion by a potent and selective
 GnRH-receptor antagonist peptide in healthy early follicular-phase women
 are mediated via selective control of LH secretory burst mass
 AU Gianotti, L.; Veldhuis, J. D.; Destefanis, S.; Lanfranco, F.; Ramunni, J.;
 Arvat, E.; Marzetto, M.; Boutignon, F.; Deghenghi, R.;
 Ghigo, E.
 CS Division of Endocrinology, Department of Internal Medicine, University of
 Turin, Turin, Italy
 SO Clinical Endocrinology (Oxford, United Kingdom) (2003), 59(4), 526-532
 CODEN: CLECAP; ISSN: 0300-0664
 PB Blackwell Publishing Ltd.
 DT Journal
 LA English
 AB Aim: GnRH antagonists are competitive inhibitors of GnRH receptors. Their
 administration induces prompt suppression of the gonadal axis. In
 animals, GnRH antagonists upregulate the activity of GnRH-secreting
 neurons, which could cause gonadotrophin rebound following inhibition.
 The aim of this study was to evaluate the effects of a potent GnRH
 antagonist, **Teverelix** (TEV), on the gonadal axis in healthy
 young women. Subjects and Measurements: In nine women [20-35 yr old, body
 mass index (BMI) 19-25 kg/m²] in the early follicular phase, serum LH and
 FSH levels were evaluated every 10 min from 08.00 to 12.00 h before, and
 24 h and 96 h after TEV injection (2.5 mg in 1 mL s.c. on day 0). Serum
 gonadotrophin and estradiol levels were also evaluated at baseline and at
 6, 8, 12, 48, 72 h after TEV. Results: The antagonist reduced both serum
 LH and FSH concns.; LH levels were significantly and promptly reduced at
 +6 h (nadir at +8 h) until +48 h and recovered at +72 h, while FSH levels
 were reduced ($P < 0.05$) 24 h after the antagonist and normalized at +48 h.
 LH (but not FSH) concns. at +96 h exceeded baseline ($P < 0.05$). TEV
 suppressed estradiol concns. ($P < 0.05$) with a nadir at +24 h, comparable
 reduction at +48 h and recovery to baseline at +72 h. Deconvolution anal.
 showed that the antagonist peptide suppressed ($P < 0.02$) the pulsatile
 production rate, burst mass and amplitude of LH on day 1. Pulsatile FSH
 secretion also fell at this time ($P < 0.05$). LH and FSH pulse frequency
 were not modified by TEV. At +96 h, LH pulsatility did not significantly
 differ from that at baseline. Suppression of mean LH or FSH concns. did
 not affect the relative pattern regularity (approx. entropy) of LH and FSH
 secretion. Conclusions: This study demonstrates that the acute
 administration of a potent GnRH antagonist induces prompt inhibition of
 the gonadal axis lasting for 2 days in women due to mechanistically
 specific suppression of LH secretory burst mass and the mean FSH secretion
 rate. The trend toward rebound release of LH following the end of the
 pharmacol. effect of the antagonist could reflect a rise in endogenous
 GnRH activity.
 IT 144743-92-0, **Teverelix**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (GnRH receptor antagonist; effects of a potent GnRH antagonist,
Teverelix, on activity of gonadal axis in healthy early
 follicular-phase women)
 IT 144743-92-0, **Teverelix**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (GnRH receptor antagonist; effects of a potent GnRH antagonist,
Teverelix, on activity of gonadal axis in healthy early
 follicular-phase women)
 RN 144743-92-0 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-
 phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-
 D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:560913 HCAPLUS
DN 140:169461
TI PLGA-PEG microspheres of **teverelix**: influence of polymer type on
microsphere characteristics and on **teverelix** in vitro release
AU Mallarde, Delphine; Boutignon, Francois; Moine, Fabien; Barre,
Edith; David, Sandrine; Touchet, Helene; Ferruti, Paolo; Deghenghi,
Romano
CS Europeptides, Argenteuil, 95108, Fr.
SO International Journal of Pharmaceutics (2003), 261(1-2), 69-80
CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier Science B.V.
DT Journal
LA English
AB **Teverelix** microspheres were produced by coacervation using a new
type of poly(ester-carbonates) made of block copolymers of
poly(lactic-glycolic acid) (PLGA) and poly(ethylene glycol) (PEG). Five
different PLGA-PEG copolymers and one PLGA were used. The stability
'window' has been determined for all polymers. It varied depending on the mol.
weight and the weight percentage of PEG. With increasing core loading (from 9.4
to 34.2%), the microparticle size increased from 10-50 to 5-1000 μm .
The core loading did not have any influence on encapsulation yield, which
remained above 80%. The influence of polymer type on microsphere
characteristics was studied at two different core loadings: 9.4 and 28%.
At a low core loading, the nature of the polymer had no influence on

microsphere characteristics whereas at 28%, only PLGA-PEG copolymers gave acceptable microparticles in term of particle size. At 28%, the glass transition temperature (Tg) of loaded particles was 1-8° higher than the Tg of the corresponding polymer. Increasing the core loading increased **teverelix** release whereas polymer degradation was decreased. All microparticles made of PLGA-PEG copolymers showed a faster release of **teverelix** than PLGA-based microspheres, whatever the core loading. One PLGA-PEG was selected on the basis of in vitro release rate for further in vivo investigations.

IT 144743-92-0, **Teverelix**
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (PLGA-PEG microspheres of **teverelix**)

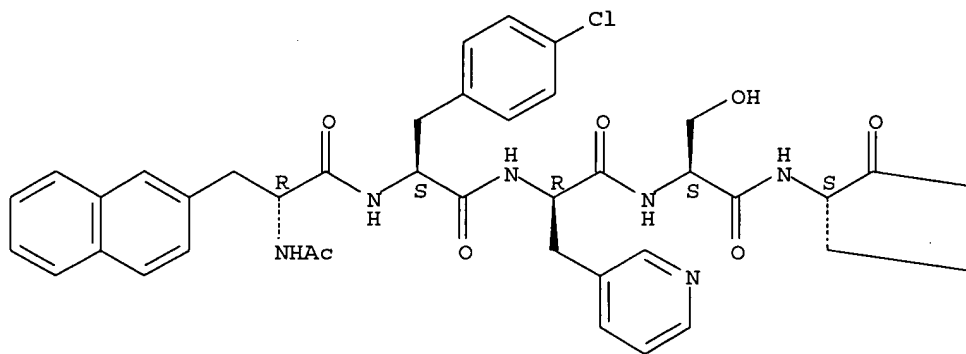
IT 144743-92-0, **Teverelix**
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (PLGA-PEG microspheres of **teverelix**)

RN 144743-92-0 HCAPLUS

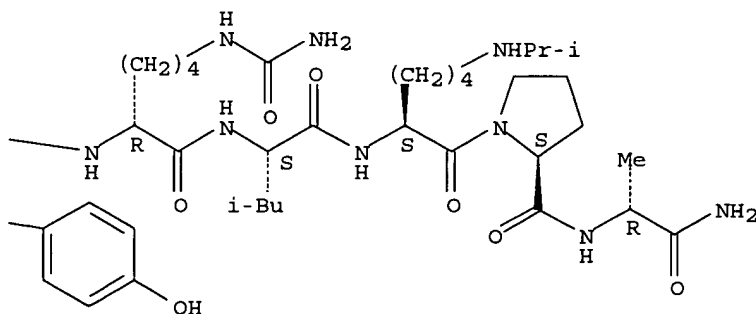
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:434387 HCAPLUS

DN 138:406980

TI Injection solutions with increased stability comprising LHRH antagonists, surfactants and a hydroxycarboxylic acid

IN Sarlikiotis, Werner; Bauer, Horst; Rischer, Matthias; Engel, Juergen; Guethlein, Frank; Di Stefano, Dominique

PA Zentaris A.-G., Germany

SO PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003045419	A1	20030605	WO 2002-EP12798	20021115
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10157628	A1	20030612	DE 2001-10157628	20011126
	EP 1448221	A1	20040825	EP 2002-790384	20021115
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
	BR 2002014412	A	20040914	BR 2002-14412	20021115
	JP 2005510544	T2	20050421	JP 2003-546920	20021115
	ZA 2004004051	A	20050408	ZA 2004-4051	20040525
	NO 2004002449	A	20040611	NO 2004-2449	20040611
PRAI	DE 2001-10157628	A	20011126		
	WO 2002-EP12798	W	20021115		

AB The aqueous injection solution comprising an LHRH antagonist contains in addition to the LHRH antagonist, such as cetrorelix, an organic, physiol. compatible acid and optionally a surfactant and carrier. The LHRH antagonist has significantly improved solubility and can be prepared in higher concns. and with an improved bioavailability. The aggregation tendency of the LHRH antagonist is significantly reduced. Thus a composition contained in 2 L water (g): cetrorelix 0.500; gluconic acid δ -lactone 2.4; Tween 80 2.0; mannite 95.0.

IT 144743-92-0, Teverelix

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(injection solns. with increased stability comprising LHRH antagonists, surfactants and a hydroxycarboxylic acid)

IT 144743-92-0, Teverelix

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

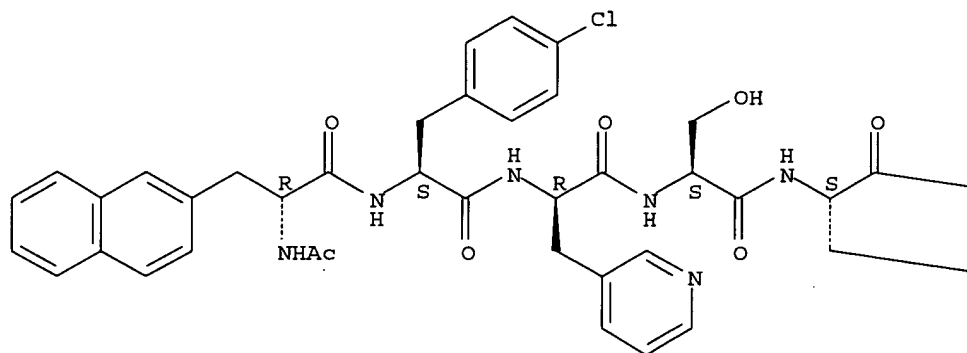
(injection solns. with increased stability comprising LHRH antagonists, surfactants and a hydroxycarboxylic acid)

RN 144743-92-0 HCAPLUS

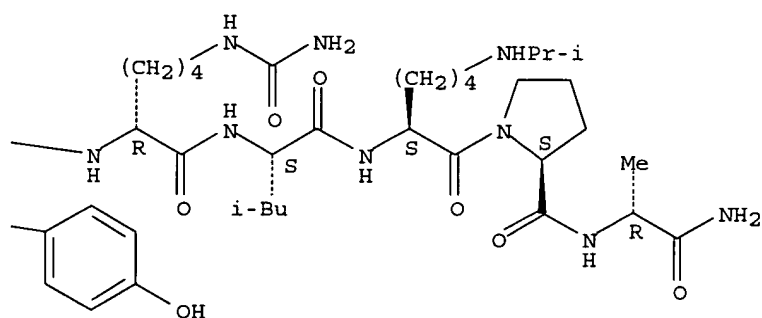
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:174240 HCAPLUS
DN 138:226729
TI Sustained release of microcrystalline peptide suspensions
IN Deghenghi, Romano; Boutignon, Francois
PA Switz.
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003044463	A1	20030306	US 2002-80130	20020219 <--
	CA 2459309	AA	20030320	CA 2002-2459309	20020827 <--
	WO 2003022243	A2	20030320	WO 2002-EP9537	20020827 <--
	WO 2003022243	A3	20031030		
	W:	AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA			
	RW:	AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR			
	EP 1423150	A2	20040602	EP 2002-772214	20020827 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002012333	A	20040921	BR 2002-12333	20020827 <--
CN 1551785	A	20041201	CN 2002-817377	20020827 <--
JP 2005504787	T2	20050217	JP 2003-526373	20020827 <--
ZA 2004001390	A	20040827	ZA 2004-1390	20040220 <--

PRAI US 2001-317616P P 20010906 <--
 WO 2002-EP9537 W 20020827

AB The invention relates to a method of preventing gel formation of a hydrophobic peptides by contacting the hydrophobic peptide with a counterion in an amount and at a molar ratio with the peptide that are sufficient to provide a fluid, milky microcryst. aqueous suspension of the peptide without formation of a gel. The invention also relates to a fluid, milky microcryst. aqueous suspension of a hydrophobic peptide and a counterion in water, wherein the peptide and counter-ion are present in amts. and at a molar ratio sufficient to form, upon mixing, the suspension without formation of a gel.

IT 500717-24-8 500717-25-9
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sustained release of microcryst. peptide suspensions)

IT 144743-92-0, Teverelix
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sustained release of microcryst. peptide suspensions)

IT 500717-24-8
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sustained release of microcryst. peptide suspensions)

RN 500717-24-8 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, trifluoroacetate (9CI) (CA INDEX NAME)

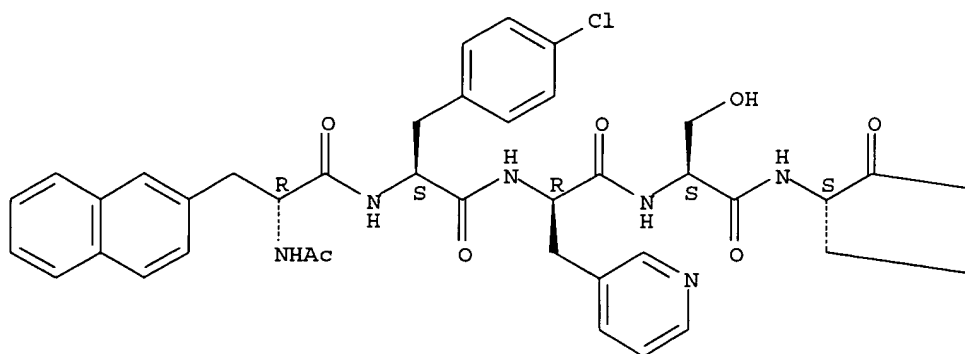
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CRN 144743-92-0

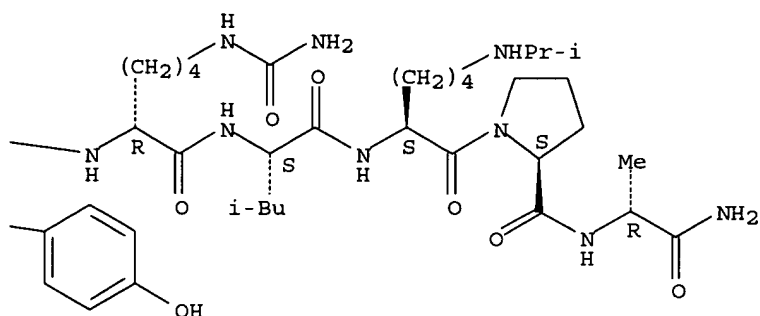
CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A



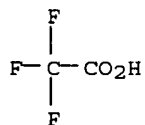
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L11 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:114201 HCAPLUS

DN 138:147717

TI Use of LHRH antagonists in non-castrating doses for the improvement of T-cell-mediated immunity

IN Engel, Jurgen; Peukert, Manfred

PA Zentaris AG, Germany

SO Ger. Offen., 2 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10137174	A1	20030213	DE 2001-10137174	20010731
	CA 2452524	AA	20030213	CA 2002-2452524	20020730
	WO 2003011314	A2	20030213	WO 2002-EP8459	20020730
	WO 2003011314	A3	20031016		
	W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
	EP 1414481	A2	20040506	EP 2002-767276	20020730
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, SK				
	US 2004138138	A1	20040715	US 2002-748887	20020730
	BR 2002011498	A	20040817	BR 2002-11498	20020730
	CN 1525865	A	20040901	CN 2002-813699	20020730
	JP 2005500348	T2	20050106	JP 2003-516544	20020730
	NZ 531263	A	20050527	NZ 2002-531263	20020730
	ZA 2003009889	A	20040219	ZA 2003-9889	20031222

Noble Jarrell

21/11/2005

PRAI DE 2001-10137174 A 20010731
 US 2001-309735P P 20010802
 WO 2002-EP8459 W 20020730

AB The invention discloses the use of LHRH antagonists in a simultaneously controlled reduction of the sex hormone level. A modification of the T-cell population is reached through use of LHRH antagonists to lower sex hormone levels. By means of controlling dosages above a castration-causative level, the desired effect on the immune system is achieved.

IT 144743-92-0, **Teverelix**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LHRH antagonists in non-castrating doses for improvement of T-cell-mediated immunity)

IT 144743-92-0, **Teverelix**

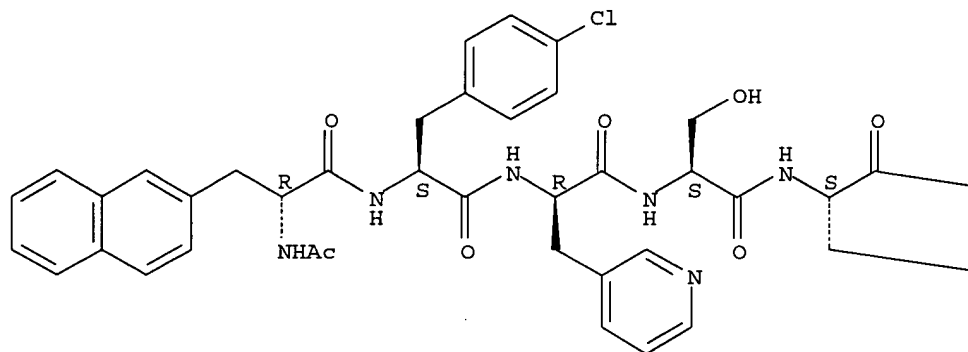
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LHRH antagonists in non-castrating doses for improvement of T-cell-mediated immunity)

RN 144743-92-0 HCAPLUS

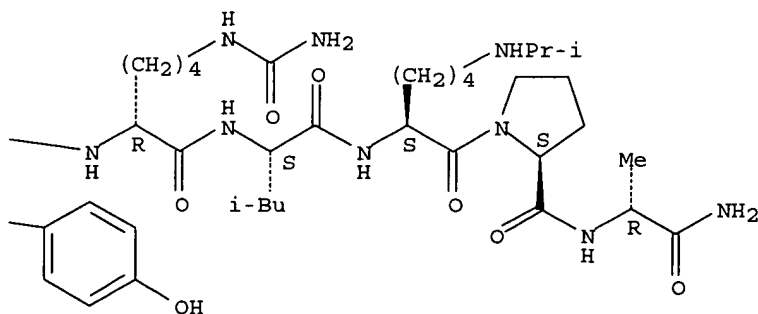
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

Noble Jarrell

21/11/2005

AN 2002:629947 HCAPLUS
 DN 138:362034
 TI Concept Evaluation: An Assay for Receptor-Mediated and Biochemical
 Antiestrogens Using Pubertal Rats
 AU Ashby, J.; Owens, W.; Deghenghi, R.; Odum, J.
 CS Syngenta Central Toxicology Laboratory, Macclesfield, SK10 4TJ, UK
 SO Regulatory Toxicology and Pharmacology (2002), 35(3), 393-397
 CODEN: RTOPLD; ISSN: 0273-2300
 PB Elsevier Science
 DT Journal
 LA English
 AB At present, assessment of chems. for receptor-mediated antiestrogenic
 activity involves inhibition of uterine growth stimulated by
 co-administration of a reference estrogen in either ovariectomized or immature
 rodents. In the present paper, we describe an alternative assay for both
 receptor-mediated and biochem. antiestrogens. The assay involves
 treatment of immature rats from postnatal (pnd) 25 or 26 for either 7 or
 14 days and monitors two benchmarks of puberty, the mean day of vaginal
 opening and the weight of the uterus, that require estrogen activity. The
 receptor-mediated antiestrogens ZM 189,154 and Faslodex (ICI 182,780), the
 aromatase inhibitor Arimidex (Anastrozole), and the GnRH inhibitor
 Antarelix were each effective in preventing uterine growth and in delaying
 vaginal opening for the course of the expts. The 5 α -reductase
 inhibitor Finasteride was inactive in the assay indicating assay
 specificity for antiestrogens. Delays in uterine growth were clearly
 evident in the 7-day expts., but assessment of vaginal opening required
 the 14-day protocol. No significant changes in body weight were observed in any
 of the expts. It is concluded that the assay holds promise as a simple
 method of detecting antiestrogens and that it is worthy of further study.

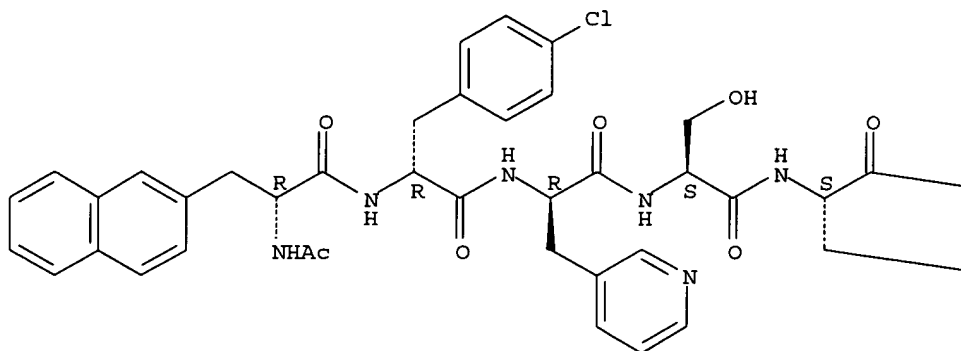
IT 151272-78-5, Antarelix
 RL: ANT (Analyte); PAC (Pharmacological activity); ANST (Analytical
 study); BIOL (Biological study)
 (antiestrogen activity determination; assay for receptor-mediated and biochem.
 antiestrogens using pubertal rats)

IT 151272-78-5, Antarelix
 RL: ANT (Analyte); PAC (Pharmacological activity); ANST (Analytical
 study); BIOL (Biological study)
 (antiestrogen activity determination; assay for receptor-mediated and biochem.
 antiestrogens using pubertal rats)

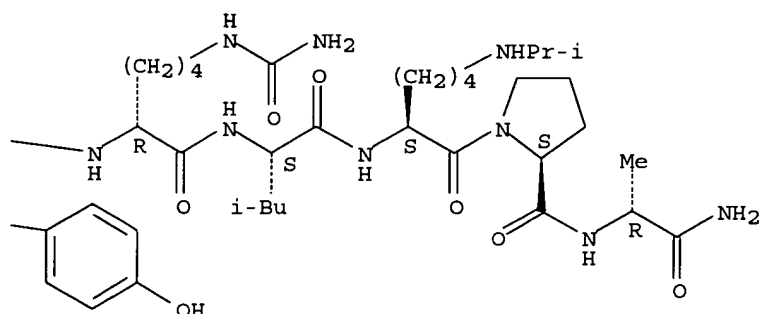
RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-
 phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-
 D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:142735 HCAPLUS

DN 136:189380

TI Method for producing peptide salts, their use, and pharmaceutical preparations containing these peptide salts in relation to cetorelix embonate

IN Damm, Michael; Salonek, Waldemar; Engel, Juergen; Bauer, Horst; Stach, Gabriele

PA Zentaris A.-G., Germany

SO PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002014347	A2	20020221	WO 2001-EP9219	20010809
	WO 2002014347	A3	20020808		
	W:			AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
	RW:			AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR	
	DE 10040700	A1	20020228	DE 2000-10040700	20000817
	AU 2002010439	A5	20020225	AU 2002-10439	20010809
	EP 1309607	A2	20030514	EP 2001-978273	20010809
	EP 1309607	B1	20041027		
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR	
	BR 2001013296	A	20030715	BR 2001-13296	20010809
	JP 2004506647	T2	20040304	JP 2002-519484	20010809
	AT 280779	E	20041115	AT 2001-978273	20010809
	NZ 524023	A	20041126	NZ 2001-524023	20010809
	EE 200300065	A	20041215	EE 2003-65	20010809
	PT 1309607	T	20050228	PT 2001-978273	20010809
	ES 2230371	T3	20050501	ES 2001-1978273	20010809
	CA 2355573	AA	20030222	CA 2001-2355573	20010822
	US 2002198146	A1	20021226	US 2001-939532	20010824
	US 6780972	B2	20040824		
	ZA 2003000777	A	20030918	ZA 2003-777	20030129
	NO 2003000618	A	20030207	NO 2003-618	20030207
	BG 107612	A	20031231	BG 2003-107612	20030306
	HK 1058366	A1	20050603	HK 2004-101030	20040213
	US 2004259801	A1	20041223	US 2004-895468	20040713

PRAI DE 2000-10040700 A 20000817
 WO 2001-EP9219 W 20010809
 US 2001-939532 A1 20010824

AB The invention relates to pharmaceutical prepsns. containing peptide salt, to their production, and to the use as injections. The invention particularly relates to pharmaceutical prepsns. containing a slightly soluble salt of LHRH agonists or antagonists such as cetorelix embonate for the parenteral administration in mammals with a long-sustained action. Thus 46.47 g D 20761 (Cetorelix acetate) was dissolved in 1193 water; 3261 g 96% ethanol was added, filtered and mixed with 390 g Amberlite MB3 (mixed-bed cation-anion-exchanger). After treatment the resin was filtered; to 4162 g of the supernatant 5.34 g embonic acid were added. 3333 G of the Cetorelix embonate solution was sterile filtered and mixed with 528 g mannitol solution (316.8 g mannite was dissolved previously in 1267 g water), sterilized and filled in ampules and lyophilized.

IT 144743-92-0, Teverelix

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (method for producing peptide salts, use, and pharmaceutical prepsns. containing peptide salts in relation to cetorelix embonate)

IT 144743-92-0, Teverelix

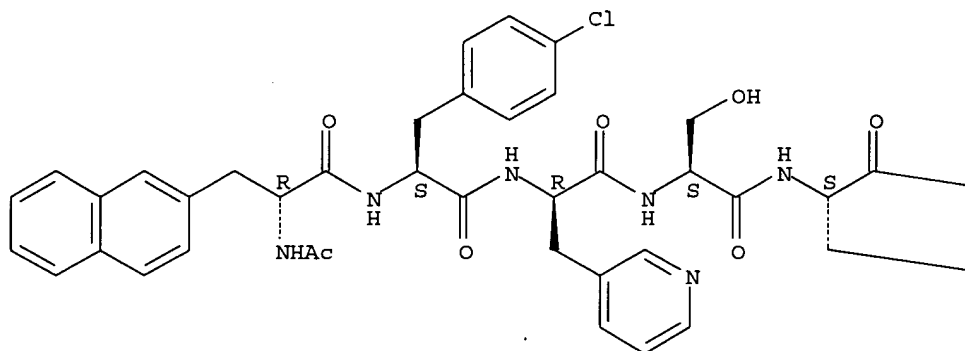
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (method for producing peptide salts, use, and pharmaceutical prepsns. containing peptide salts in relation to cetorelix embonate)

RN 144743-92-0 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Chemical structure of a complex molecule, likely a peptide derivative. The structure shows a central chain with various side groups, including a 4-hydroxyphenyl group, a 4-aminophenyl group, a 4-methylphenyl group, and a 4-aminophenyl group. The chain is linked by amide bonds and includes a thioether linkage. Stereochemistry is indicated with 'S' and 'R' labels. A label 'NHPr-i' is present near the 4-aminophenyl group.

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2001087265	A2	20011122	WO 2001-EP5555	20010516
	WO 2001087265	A3	20020418		
	W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	DE 10024451	A1	20011129	DE 2000-10024451	20000518
	EP 1282400	A2	20030212	EP 2001-940482	20010516
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
	BR 2001010892	A	20030311	BR 2001-10892	20010516
	JP 2003533466	T2	20031111	JP 2001-583734	20010516
	NZ 522381	A	20040730	NZ 2001-522381	20010516
	AU 777185	B2	20041007	AU 2001-74041	20010516
	RU 2253438	C2	20050610	RU 2002-134463	20010516
	CA 2348167	AA	20011118	CA 2001-2348167	20010518
PRAI	US 2002039996	A1	20020404	US 2001-861009	20010518
	ZA 2002008761	A	20021129	ZA 2002-8761	20021030
	BG 107312	A	20030630	BG 2002-107312	20021125
	US 2005159335	A1	20050721	US 2005-28875	20050104
	DE 2000-10024451	A	20000518		
	WO 2001-EP5555	W	20010516		
	US 2001-861009	A3	20010518		

IT 151272-78-5, Antarelix
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic

use); BIOL (Biological study); PROC (Process); USES (Uses)
(formulation of parenteral peptide drugs to prevent aggregation)

IT 151272-78-5, Antarelix

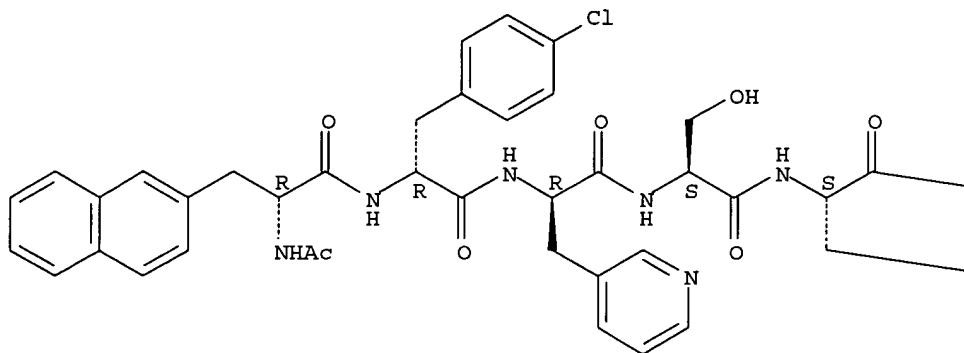
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(formulation of parenteral peptide drugs to prevent aggregation)

RN 151272-78-5 HCAPLUS

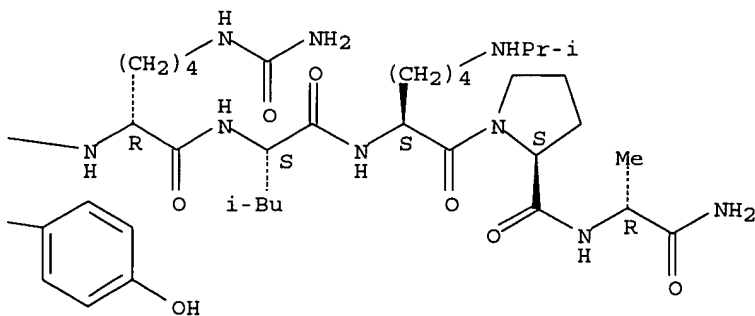
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:757132 HCAPLUS

DN 136:96187

TI Replacement of surgical castration by GnRH-inhibition or Leydig cell ablation in the male rat Hersherberger antiandrogen assay

AU Ashby, J.; Lefevre, P. A.; Deghenghi, R.; Wallis, N.

CS Syngenta Central Toxicology Laboratory, Macclesfield, Cheshire, SK10 4TJ, UK

SO Regulatory Toxicology and Pharmacology (2001), 34(2), 188-203

CODEN: RTOPDW; ISSN: 0273-2300

PB Academic Press

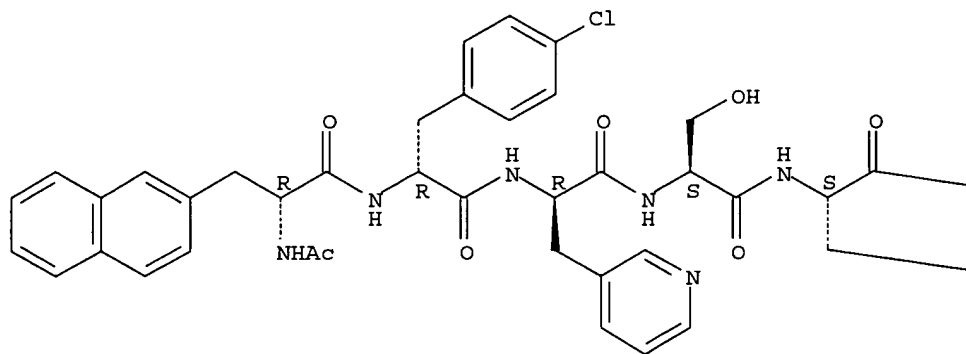
DT Journal

LA English

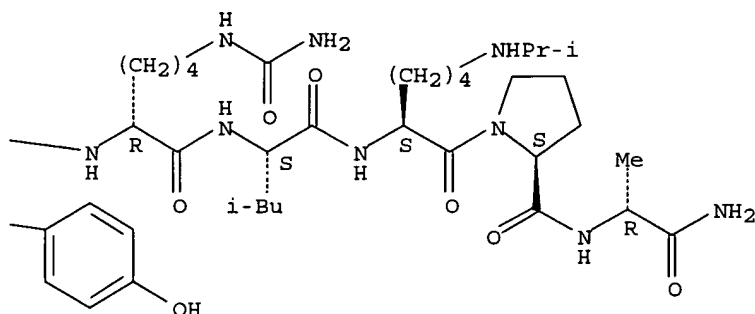
- AB An obstacle to the widespread adoption of the Hershberger antiandrogen assay is the surgical castration procedure required to produce androgen deficiency in the test animals. Here the authors describe two chemical treatments that produce similar effects to surgical castration. The first is use of ethane dimethane sulfonate (EDS), a specific toxin to the testosterone-producing Leydig cells of the mature testes. The second class of compound is the decapeptide inhibitors of the gonadotrophin-releasing hormone (GnRH), compds. such as Antarelix and Antide. Administration of either EDS or the GnRH inhibitors results in loss of weight of the testes, epididymides, and sex-associated tissues. Co-administration of testosterone to these animals leads to reversal of the induced effects. The basic test protocol for both of these assay modifications is described. Flutamide was used as a representative potent antiandrogen, and DDE as an example of a weakly active antiandrogen. The 5 α -reductase inhibitor finasteride was used to inhibit the transformation of testosterone to dihydrotestosterone. It is shown that the EDS assay is sensitive to the antiandrogen flutamide, but that it fails to detect the weaker antiandrogen DDE. In contrast, the Antarelix assay performs as well as does the classical castration assay, leading to the detection as antiandrogens of flutamide, DDE, and finasteride. It is concluded that the GnRH inhibition Hershberger assay is more convenient to conduct than the original surgical castration assay, and it involves less stress to the test animals. (c) 2001 Academic Press.
- IT 151272-78-5, Antarelix
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(replacement of surgical castration by GnRH-inhibition or Leydig cell ablation in male rat Hershberger antiandrogen assay)
- IT 151272-78-5, Antarelix
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(replacement of surgical castration by GnRH-inhibition or Leydig cell ablation in male rat Hershberger antiandrogen assay)
- RN 151272-78-5 HCAPLUS
- CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:731316 HCAPLUS
DN 135:262286
TI Compressed microparticles for dry injection
IN Boutignon, Francois
PA Fr.
SO U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Ser. No. 491,978,
abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001026804	A1	20011004	US 2001-764111	20010119
	US 6627600	B2	20030930		
PRAI	AU 2000-22	A	20000118		
	US 2000-491978	B2	20000127		

AB The invention relates to a pharmaceutical implant for controlled release of drug and methods for manufacturing and administering the implant. The implant is made of associated microparticles of a drug dispersed in a biodegradable polymer. The microparticles are sufficiently associated so that the implant maintains a predetd. shape but are not fused together so as to form a single monolithic structure. The drug can be released in a controlled-release manner by administration of the implant without the need of a suspending fluid. Implants were made of microparticles containing the peptide **Teverelix**, and each microparticle contained 25% **Teverelix**. The microparticles were obtained by extrusion followed by grinding. The resulting pharmaceutical implant was about 1.2 cm in length and had a diameter of about 0.2 cm.

IT 144743-92-0, **Teverelix**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compressed microparticles for dry injection)

IT 144743-92-0, **Teverelix**

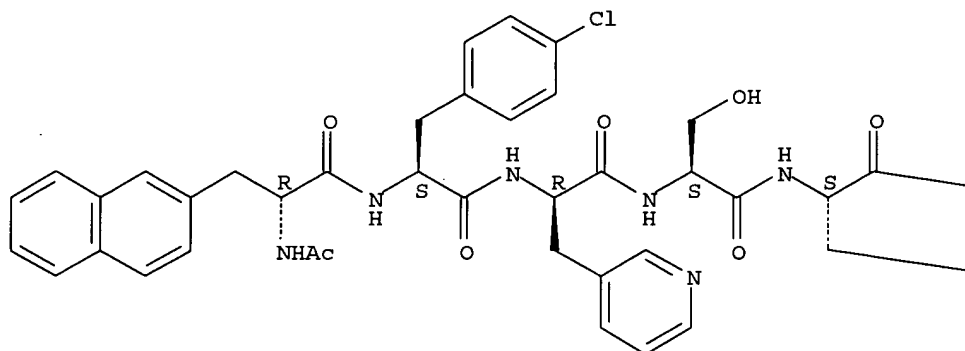
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compressed microparticles for dry injection)

RN 144743-92-0 HCAPLUS

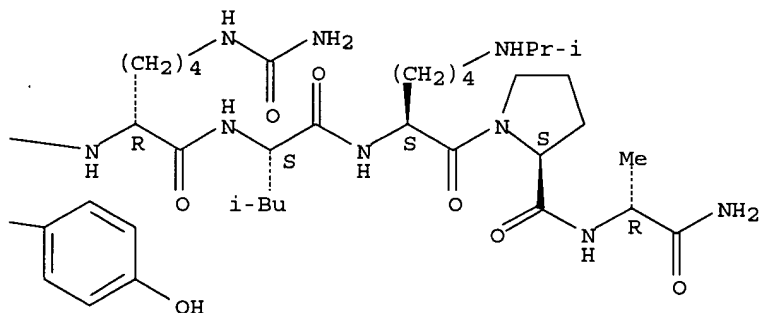
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:693347 HCAPLUS

DN 135:278010

TI LHRH-antagonists for pharmaceuticals

IN Bernd, Michael; Kutscher, Bernhard; Guenther, Eckhard; Romeis, Peter;
Reissmann, Thomas; Beckers, Thomas

PA Zentaris A.-G., Germany

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA German

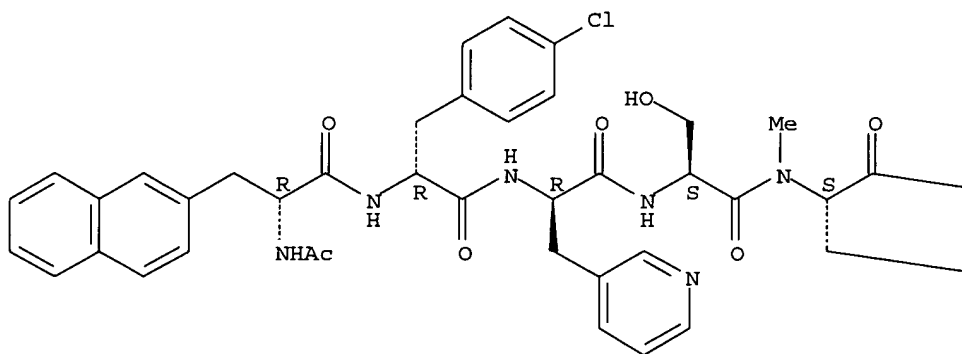
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001068676	A2	20010920	WO 2001-EP2719	20010312
	WO 2001068676	A3	20021024		
	W:				
	AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	US 6627609	B1	20030930	US 2000-525007	20000314
	CA 2402193	AA	20020909	CA 2001-2402193	20010312
	BR 2001009279	A	20021217	BR 2001-9279	20010312
	EP 1268522	A2	20030102	EP 2001-933682	20010312
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

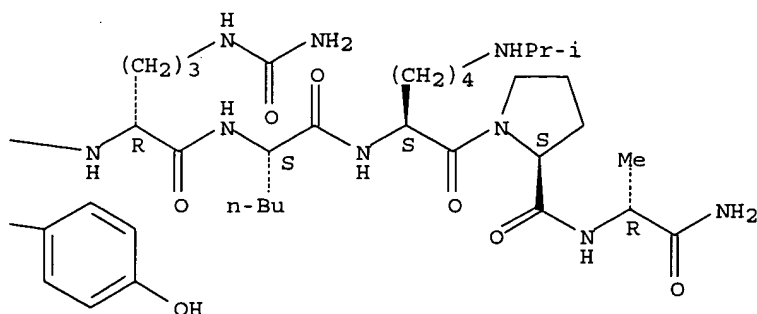
JP 2003535044	T2	20031125	JP 2001-567766	20010312
NZ 521273	A	20050128	NZ 2001-521273	20010312
RU 2248982	C2	20050327	RU 2002-127786	20010312
ZA 2002007248	A	20030221	ZA 2002-7248	20020910
NO 2002004363	A	20021113	NO 2002-4363	20020912
BG 107121	A	20030530	BG 2002-107121	20020918
US 2004266695	A1	20041230	US 2003-671573	20030929
PRAI US 2000-525007	A	20000314		
DE 1999-19911771	A	19990317		
WO 2001-EP2719	W	20010312		
OS		MARPAT 135:278010		
AB	The invention relates to peptides comprising an N-methylated amino acid component and an improved water solubility Compns. containing the peptides can be used for treatment of hormone-dependent tumors and hormone-induced non-malignant disease states. Thus, a decapeptide was prepared, and a solution of this peptide (1.62 g) in 30% HOAc was diluted with 1.5-L water. To the above solution was added 82.2 g D-mannitol and the whole solution was sterile filtered.			
IT	361432-27-1P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (LHRH-antagonists for pharmaceuticals)			
IT	361432-27-1P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (LHRH-antagonists for pharmaceuticals)			
RN	361432-27-1 HCAPLUS			
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N-methyl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-norleucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)			

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:564807 HCAPLUS

DN 135:142239

TI Compressed microparticles for dry injection

IN Boutignon, Francois

PA Asta Medica A.-G., Germany

SO PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001054662	A2	20010802	WO 2001-EP733	20010124
	WO 2001054662	A3	20020321		
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	CA 2398533	AA	20010802	CA 2001-2398533	20010124
	AU 2001040536	A5	20010807	AU 2001-40536	20010124
	AU 779938	B2	20050217		
	BR 2001007874	A	20021105	BR 2001-7874	20010124
	EP 1263416	A2	20021211	EP 2001-911519	20010124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
	JP 2003521491	T2	20030715	JP 2001-555641	20010124
	NZ 520245	A	20040827	NZ 2001-520245	20010124
	NO 2002003399	A	20020910	NO 2002-3399	20020715
PRAI	US 2000-491978	A	20000127		
	WO 2001-EP733	W	20010124		

AB The invention relates to a pharmaceutical implant for controllably releasing a drug in a subject and methods for manufacturing and administering the implant. The implant is made of associated microparticles of a drug dispersed in a biodegradable polymer. The microparticles are sufficiently associated so that the implant maintains a predetd. shape but are not fused together so as to form a single monolithic structure. The drug can be controllably released in a subject by administration of the pharmaceutical implant without the need of a suspending fluid. Implants (1.2 cm length and 0.2 cm diameter) made of microparticles containing 25% peptide Teverelix were prepared. Effect of particle size on in vitro release of Teverelix was studied.

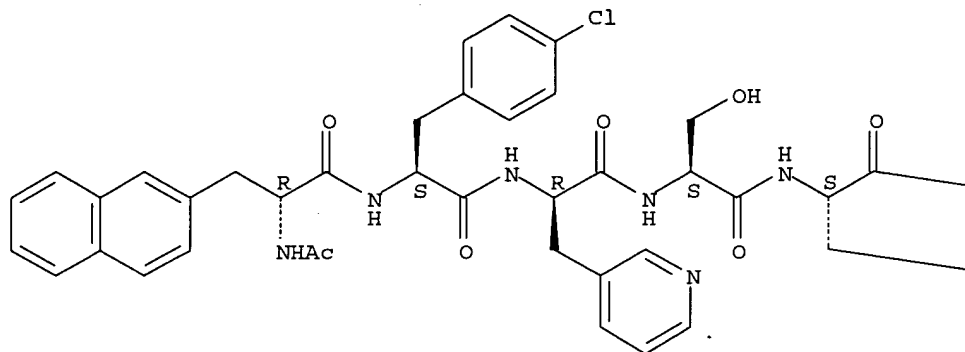
IT 144743-92-0, Teverelix

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compressed microparticles for dry injection)

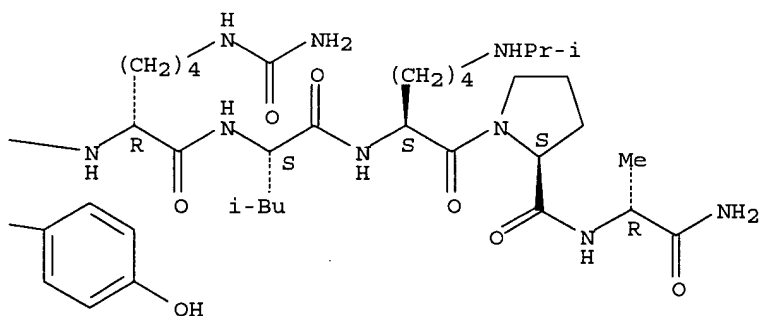
IT 144743-92-0, **Teverelix**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compressed microparticles for dry injection)
 RN 144743-92-0 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

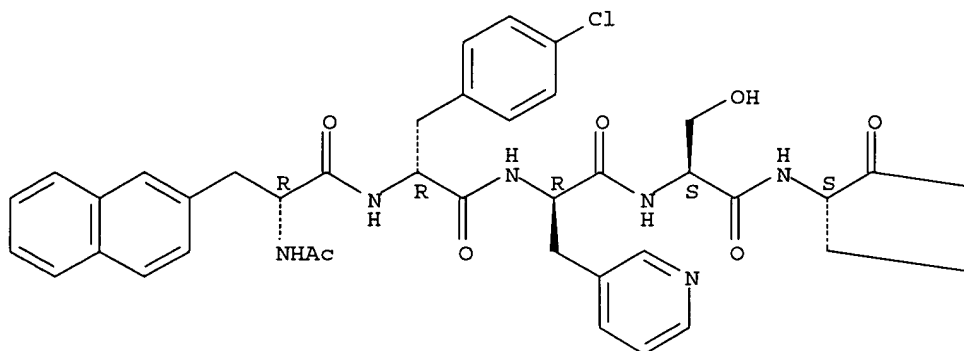


L11 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:894792 HCAPLUS
 DN 134:141823
 TI New LHRH antagonists with enhanced biological activity: Preclinical and clinical results
 AU Kutscher, Bernhard; Bernd, Michael; Gunther, Eckhard; Deger, Wolfgang; Reissmann, Thomas; Beckers, Thomas; Deghenghi, Romano; Engel, Jurgén
 CS Corporate Research, ASTA Medica AG, Frankfurt, D-60314, Germany
 SO Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 655-657. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
 CODEN: 69ATHX
 DT Conference; General Review

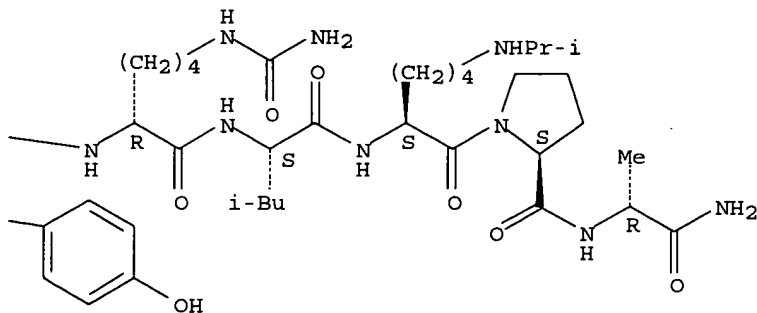
LA English
 AB A brief review/discussion with 4 refs. on the title topic with focus on Cetrorelix, Antarelix, and D-26344 and their use in treating sex hormone-dependent tumors and nonmalignant conditions.
 IT 151272-78-5, Antarelix
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (preclin. and clin. results for new LHRH antagonists with enhanced biol. activity)
 IT 151272-78-5, Antarelix
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (preclin. and clin. results for new LHRH antagonists with enhanced biol. activity)
 RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



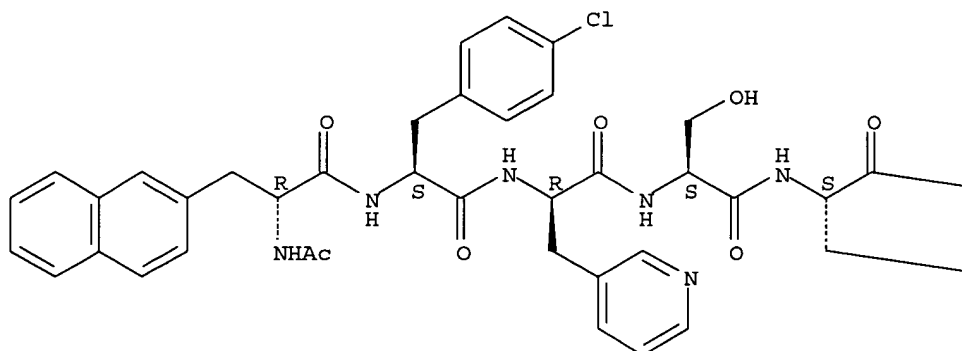
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

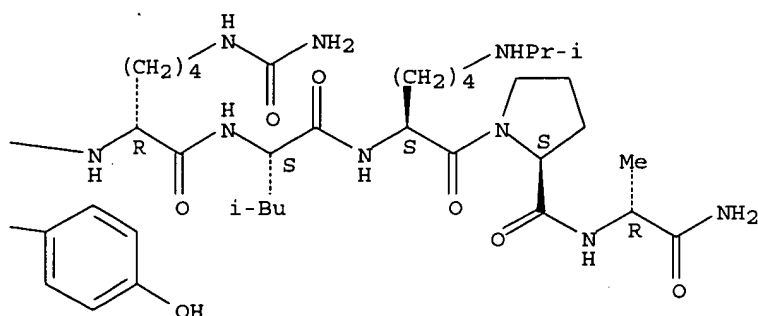
AN 2000:842881 HCAPLUS
 DN 134:125682
 TI LHRH antagonists: New preclinical and clinical results
 AU Kutscher, B.; Bernd, M.; Deger, W.; Reissmann, T.; Deghenghi, R.; Engel, J.
 CS Corporate Research and Development ASTA Medica AG, Dresden, Germany
 SO Peptides: Biology and Chemistry, Proceedings of the Chinese Peptide Symposium, 5th, Lanzhou, China, July 14-17, 1998 (2000), Meeting Date 1998, 264-268. Editor(s): Hu, Xiao-Yu; Wang, Rui; Tam, James P. Publisher: Kluwer Academic Publishers, Dordrecht, Neth. CODEN: 69AQX6
 DT Conference
 LA English
 AB **Teverelix** and D-26344, a D-Lys-6-analog of Cetrorelix, show excellent human LHRH-receptor affinity, long lasting testosterone suppression in rats up to 648 h (D-26344), and minimal histamine release. Both compds. are in preclin. evaluation for treatment of sex-hormone dependent tumors. Several nonmalignant conditions such as benign prostatic hyperplasia are also possibly appreciable targets for these LHRH antagonists.
 IT **144743-92-0, Teverelix**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LHRH antagonists in relation to new preclin. and clin. results)
 IT **144743-92-0, Teverelix**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LHRH antagonists in relation to new preclin. and clin. results)
 RN 144743-92-0 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



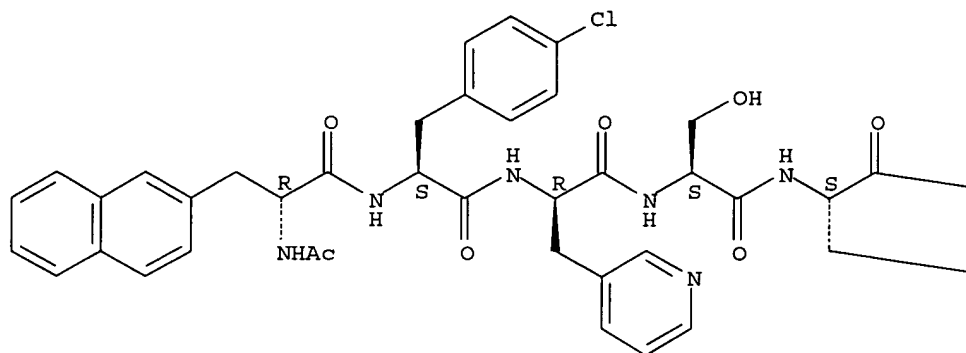
PAGE 1-B



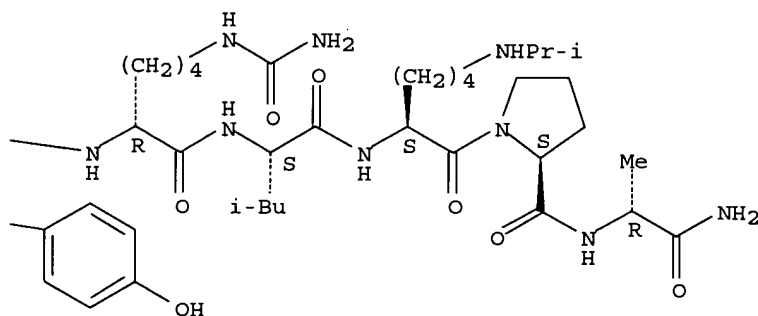
L11 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1999:722421 HCAPLUS
 DN 132:255913
 TI Sustained release formulation of the GnRH antagonist **teverelix**:
 in vivo and in vitro results
 AU Boutignon, F.; Touchet, H.; Moine, F.; Mallarde, D.; David, S.;
 Deghenghi, R.
 CS Europeptides, Argenteuil, 95108, Fr.
 SO Proceedings of the International Symposium on Controlled Release of
 Bioactive Materials (1999), 26th, 663-664
 CODEN: PCRMEY; ISSN: 1022-0178
 PB Controlled Release Society, Inc.
 DT Journal
 LA English
 AB The in vitro release of **teverelix** from microgranules over 45
 days was studied. After a 24-h burst of about 15%, the peptide release
 followed a zero-order release throughout the study. The pharmacokinetics
 profile was very similar to the in vitro dissoln. profile.
 IT 144743-92-0, **Teverelix**
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); THU (Therapeutic use);
 BIOL (Biological study); PROC (Process); USES (Uses)
 (sustained release formulation of GnRH antagonist **teverelix**)
 IT 144743-92-0, **Teverelix**
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); THU (Therapeutic use);
 BIOL (Biological study); PROC (Process); USES (Uses)
 (sustained release formulation of GnRH antagonist **teverelix**)
 RN 144743-92-0 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-
 phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-
 D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

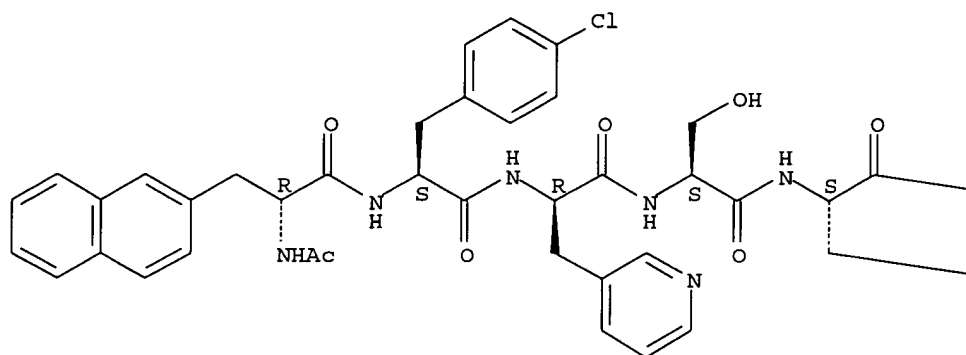
L11 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:169441 HCAPLUS
DN 128:235145
TI Pharmaceutical implants containing bioactive peptides
IN Deghenghi, Romano
PA Deghenghi, Romano, Switz.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809613	A1	19980312	WO 1997-EP4095	19970728
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945128	A	19990831	US 1997-897942	19970721
CA 2236595	AA	19980312	CA 1997-2236595	19970728

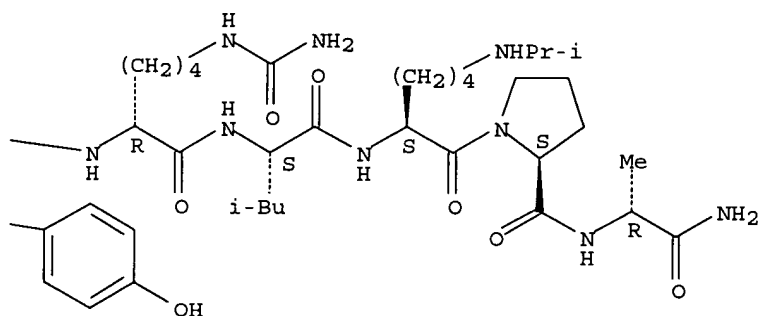
AU 9740121	A1	19980326	AU 1997-40121	19970728
AU 713123	B2	19991125		
EP 858323	A1	19980819	EP 1997-937521	19970728
EP 858323	B1	20040331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1200032	A	19981125	CN 1997-191184	19970728
BR 9706741	A	19990720	BR 1997-6741	19970728
JP 11514678	T2	19991214	JP 1998-512154	19970728
AT 262889	E	20040415	AT 1997-937521	19970728
PT 858323	T	20040831	PT 1997-937521	19970728
ES 2218696	T3	20041116	ES 1997-937521	19970728
US 6077523	A	20000620	US 1999-311744	19990514
US 6159490	A	20001212	US 2000-543707	20000405
PRAI US 1996-25444P	P	19960904		
US 1997-897942	A	19970721		
WO 1997-EP4095	W	19970728		
US 1999-311744	A1	19990514		
AB	A process for manufacturing a pharmaceutical composition for the delivery of an effective amount of a bioactive peptide or peptide analog over a period of 1 to 12 mo is disclosed. This process includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 μ m; sterilizing the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing γ -radiation; wetting the ground and sterilized copolymer with a sterile aqueous slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixture of the copolymer and between about 10 and 50 % of the bioactive peptide or peptide analog; drying the mixture at reduced pressure and at temperature not exceeding 25°C; aseptically extruding the dried mixture at a temperature between about 70 and 110°C; and aseptically cutting cylindrical rods of about 1 to 2 mm diameter and between about 10 and 25 mm in length from the extruded mixture to form the pharmaceutical implants. Pharmaceutical rods for s.c. implant, 1.5 mm diameter and 15 mm long, containing 10 mg avorelin were prepared according to above method and were implanted in dogs. After the initial stimulation of LH and testosterone, castration levels of testosterone were maintained for 6 mo. The plasma levels of avorelin, after a short-lived burst, fell to a nadir at 40 day days and rose again at 120 days before becoming undetectable at day 160.			
IT	144743-92-0D, Teverelix, salts RL: BSU (Biological study, unclassified); BIOL (Biological study) (pharmaceutical implants containing bioactive peptides)			
IT	144743-92-0D, Teverelix, salts RL: BSU (Biological study, unclassified); BIOL (Biological study) (pharmaceutical implants containing bioactive peptides)			
RN	144743-92-0 HCAPLUS			
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)			

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:39510 HCAPLUS

DN 128:149663

TI GnRH secretion into CSF in rams treated with a GnRH antagonist

AU Blache, D.; Chagas, L. M.; Caraty, A.; Deghenghi, R.; Delaleu, B.; Blackberry, M. A.; Martin, G. B.

CS Faculty Agriculture (Animal Science), University Western Australia, Nedlands, 6907, Australia

SO Journal of Neuroendocrinology (1997), 9(12), 887-892

CODEN: JOUNE2; ISSN: 0953-8194

PB Blackwell Science Ltd.

DT Journal

LA English

AB The equilibrium of the brain-pituitary-testicular axis is controlled by neg. feedback exerted primarily through changes in the circulating concns. of gonadal steroids. This is usually studied in gonadectomized animals treated with single large doses or constant low levels of exogenous steroid. However, the feedback system probably also contains dynamic components, perhaps expressed as delays to changes in GnRH secretion following a change in steroid concentration. These delays must be measured without interference from surgical procedures, including anesthesia, bias associated with changes in pituitary responsiveness (which affect the efficiency of pulse detection), and chronic side-effects of gonadectomy. We used a GnRH antagonist ['Antarelix': Ac-D-Nal, D-Cpa, D-Pal, Ser, Tyr, D-Hci, Leu,

Lys-(iPr), Pro, D-Ala-NH₂] to transiently block LH and steroid secretion (in effect, inducing and reversing castration) in mature male sheep, and measured GnRH secretion into cerebrospinal fluid (CSF) in the third cerebral ventricle. The CSF was withdrawn with a peristaltic pump at a rate of 2 mL/h and pooled every 20 min. Jugular plasma was sampled every 20 min and analyzed for testosterone and LH pulses. The antagonist (500 µg i.v.) was injected after 6 h of baseline sampling and the study continued for a further 24 h. The pulses of LH and testosterone disappeared shortly after antagonist injection, with delays of 20±12 min for LH and 80±29 min for testosterone. This led to an increase in GnRH pulse frequency, starting 300±54 min after antagonist injection. Secretion of LH and testosterone pulses resumed at 553±38 and 530±30 min (after antagonist injection), and GnRH pulse frequency returned to baseline values after 170±42 min (relative to LH) and 117±35 min (relative to testosterone). The consistent nature of these responses across the group of animals suggests that this can be used to test the effects of exteroceptive factors on the dynamics of neg. feedback.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(GnRH secretion into the cerebrospinal fluid in rams treated with a GnRH antagonist to study the neg. feedback dynamics of the hypothalamus-pituitary-testes axis)

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

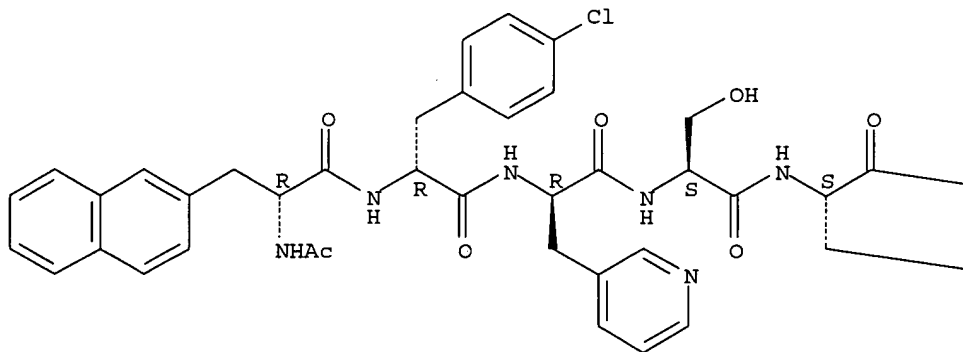
(GnRH secretion into the cerebrospinal fluid in rams treated with a GnRH antagonist to study the neg. feedback dynamics of the hypothalamus-pituitary-testes axis)

RN 151272-78-5 HCAPLUS

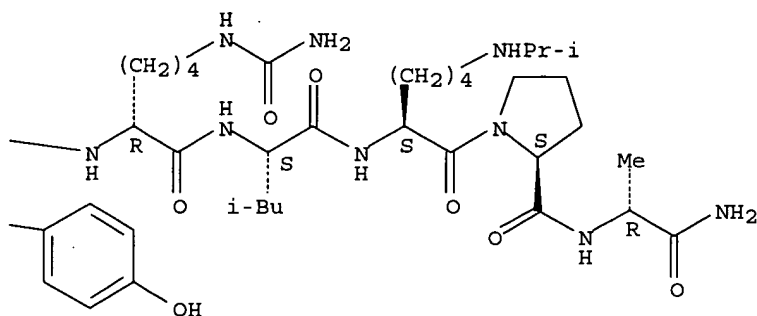
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

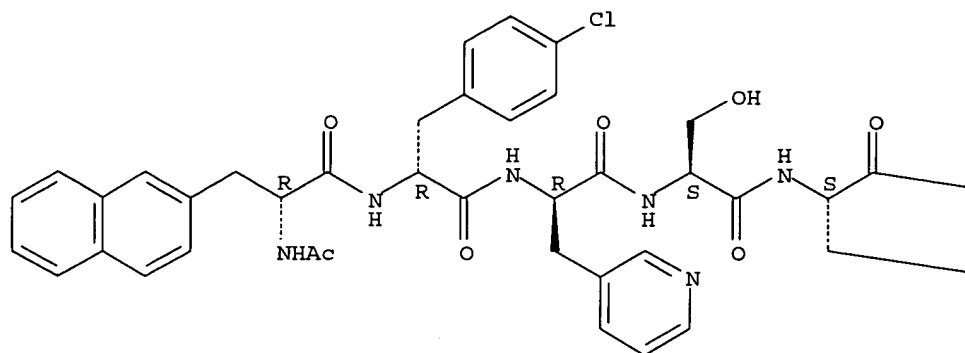


RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

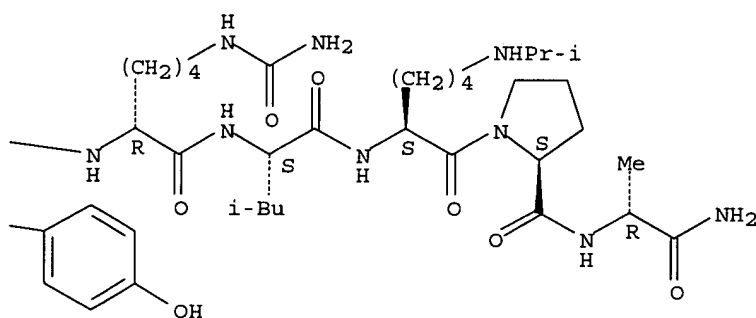
L11 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:359808 HCAPLUS
DN 127:39570
TI Antarelix
AU Deghenghi, R.
CS UK
SO Treatment with GnRH Analogs: Controversies and Perspectives, Proceedings of a Satellite Symposium of the 15th World Congress on Fertility and Sterility, Bologna, Sept. 15-16, 1995 (1996), Meeting Date 1995, 89-91. Editor(s): Filicori, Marco; Flamigni, Carlo. Publisher: Parthenon Publishing, London, UK. CODEN: 64KRAZ
DT Conference; General Review
LA English
AB A review discussion with 8 refs. on physicochem. aspects, histamine release determination and measurement of plasma levels of Antarelix, a gonadotropin-releasing hormone antagonist.
IT 151272-78-5, Antarelix
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (properties and pharmacol. and bioavailability of antarelix)
IT 151272-78-5, Antarelix
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (properties and pharmacol. and bioavailability of antarelix)
RN 151272-78-5 HCAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L11 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:306215 HCAPLUS

DN 126:339039

TI Initiation of high dose gonadotropin-releasing hormone antagonist treatment during the late follicular phase in the macaque abolishes luteal function irrespective of effects upon the luteinizing hormone surge

AU Fraser, H.M.; Lunn, S.F.; Morris, K.D.; Deghenghi, R.

CS MRC Reproductive Biology Unit, Centre for Reproductive Biol., Edinburgh, EH9 3EW, UK

SO Human Reproduction (1997), 12(3), 430-435

CODEN: HUREEE; ISSN: 0268-1161

PB Oxford University Press

DT Journal

LA English

AB The determination of the efficacy of gonadotrophin-releasing hormone (GnRH) antagonists in blocking the LH surge and luteal function is important for our understanding of the control of the menstrual cycle and for clin. application. GnRH antagonist have failed to block the LH surge reliably in the non-human primate. The aim of the study was to utilize high dose GnRH antagonist treatment administered during the late follicular phase of the menstrual cycle to block the preovulatory LH surge. It was postulated that the LH surge would be prevented in all animals, but if this failed subsequent luteal function would be blocked by continued suppression of LH, since the early corpus luteum is susceptible to inhibition by GnRH antagonist treatment. A group of 16 adult female stump-tailed macaques (*Macaca arctoides*) with regular menstrual cycles were selected. The GnRH

antagonist [N-Ac-D-Nal(2)1,D-pCl-Phe2,D-Pal(3)3,D-(Hci)6-,Lys(iPr)8,D-Ala10]GnRH (Antarelix) (concentration 10 mg/mL) was administered as three daily s.c. injections, at 1 dose of 1 mg/kg on days 11, 12 and 13 of the follicular phase of the menstrual cycle. Of nine macaques in which it was judged that the treatment was commenced within 1 day of the expected LH surge (serum estradiol >400 pmol/l), six demonstrated a decline in serum estradiol concns., a total block of the LH/FSH surge and inhibition of ovulation as judged by an absence of a rise in progesterone concns. In the three other animals in this category, a partial LH surge occurred, but this failed to result in a functional corpus luteum. In a further three animals treatment was initiated on the day of the LH surge, and again there was absence of a subsequently functional corpus luteum. These results show that GnRH is involved at the time of the mid-cycle LH/FSH surge in the non-human primate. Initiation of high dose GnRH antagonist treatment during the periovulatory period abolishes luteal function irresp. of its effects upon the LH surge because of its long-term action and resultant withdrawal of luteal support.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(LH-RH antagonist treatment during late follicular phase abolishes luteal function independent of LH surge in stump-tailed macaques)

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

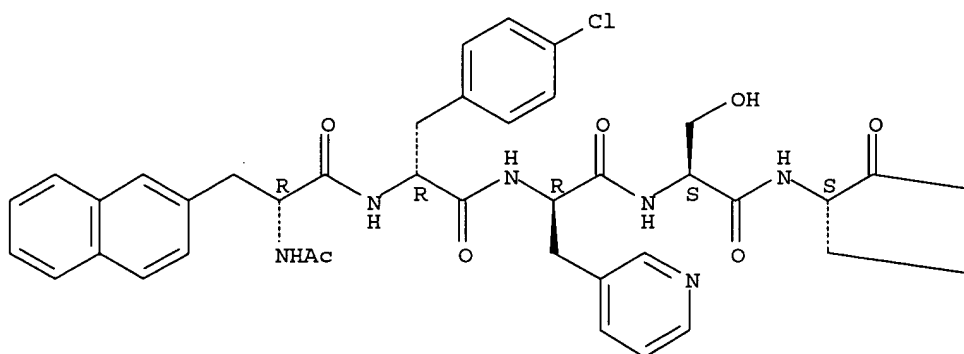
(LH-RH antagonist treatment during late follicular phase abolishes luteal function independent of LH surge in stump-tailed macaques)

RN 151272-78-5 HCAPLUS

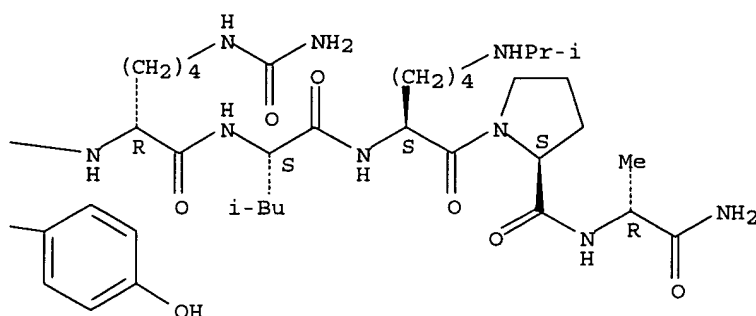
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



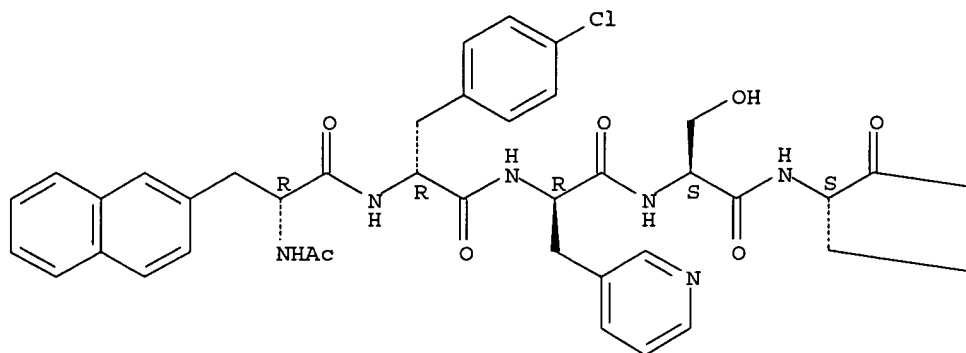
PAGE 1-B



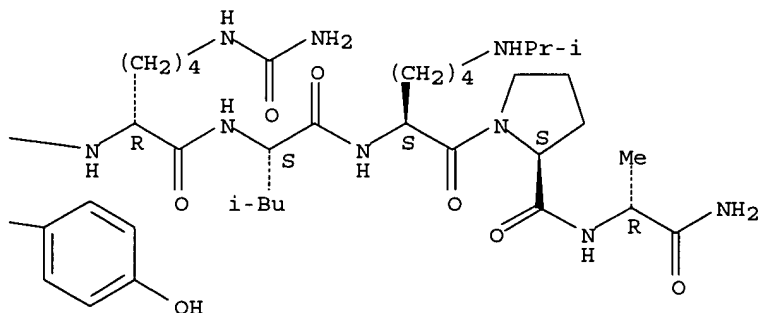
- L11 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1996:481004 HCAPLUS
 DN 125:157641
 TI Radioimmunoassay of Antarelix a luteinizing hormone releasing-hormone antagonist, in plasma and its application for pharmacokinetic study in dogs
 AU Sorensen, Suzie; Rondeau, Jean-Jacques; Lenaerts, Vincent; Boutignon, Francois; Wuethrich, Patrick; Deghenghi, Romano; Adam, Albert; Ong, Huy
 CS Fac. Pharm., Univ. Montreal, Montreal, QC, Can.
 SO Journal of Immunoassay (1996), 17(3), 205-226
 CODEN: JOUIDK; ISSN: 0197-1522
 PB Dekker
 DT Journal
 LA English
 AB A procedure for the RIA of AntarelixTM (teverelix) in plasma has been developed for the pharmacokinetic study of this potent LHRH antagonist in dogs. Antiserum was produced by coupling the deamidated Antarelix analog to bovine serum albumin by a carbodiimide reaction and immunizing rabbits with the conjugate. The cross-reactivity of the antiserum with LHRH, LHRH agonist Metereline and LHRH antagonists tested was negligible, except for Antide which displayed a cross-reactivity of 33%. No cross-reactivity with Antarelix metabolites could be detected. The RIA is suitable for the direct determination of Antarelix in plasma, with a min. detectable level of 1.12 fmol/assay. The accuracy and precision of the method were assessed with plasma samples spiked with Antarelix at concns. ranging from 0.4 to 6.4 pmol/mL. The recovery with 104.8% with intra- and interassay CV between 1 and 3.7%. Pharmacokinetic profiles of Antarelix in dogs were established following an IV or a SC dose of 10 µg/kg.
 IT 151272-78-5, Antarelix
 RL: ANT (Analyte); ANST (Analytical study)
 (RIA of Antarelix in plasma and its application for pharmacokinetic study in dogs)
 IT 151272-78-5, Antarelix
 RL: ANT (Analyte); ANST (Analytical study)
 (RIA of Antarelix in plasma and its application for pharmacokinetic study in dogs)
 RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

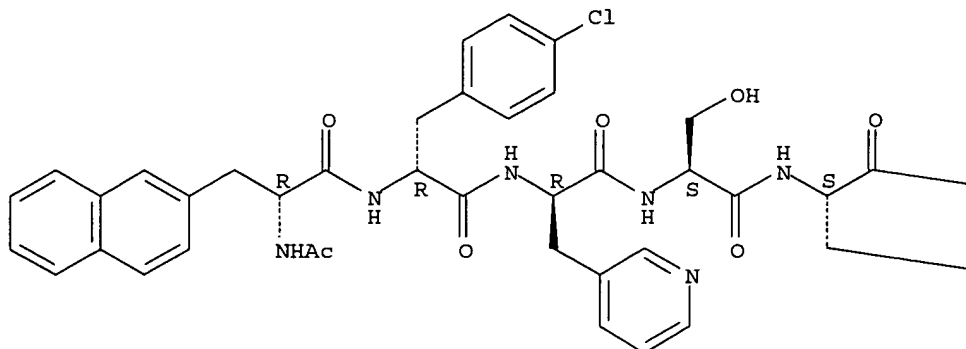


L11 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1993:641607 HCAPLUS
 DN 119:241607
 TI Antarelix (EP 24332) a novel water soluble LHRH antagonist
 AU Deghenghi, R.; Boutignon, F.; Wuthrich, P.; Lenaerts, V.
 CS Europeptides, Argenteuil, 95108, Fr.
 SO Biomedicine & Pharmacotherapy (1993), 47(2-3), 107-10
 CODEN: BIPHEX; ISSN: 0753-3322
 DT Journal
 LA English
 AB Antarelix (Ac-D-Nal,D-Cpa,D-Pal,Ser,Tyr,D-Hci,Leu,Lys-(iPr),Pro,D-Ala-NH₂) was an effective antioviulatory agent in the female rat s.c., suppressed testosterone secretion in the male rat i.m., suppressed LH in the castrate ram model i.v., was devoid of anaphylactic reaction in rats i.v., and had modest histamine-releasing effects of rat mast cells in vitro. The potency, modest histamine-liberating activity, and high water solubility indicated the potential for further development of Antarelix as an LH-RH antagonist.
 IT 151272-78-5, Antarelix
 RL: BIOL (Biological study)
 (as LH-RH antagonist)
 IT 151272-78-5, Antarelix
 RL: BIOL (Biological study)
 (as LH-RH antagonist)
 RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-

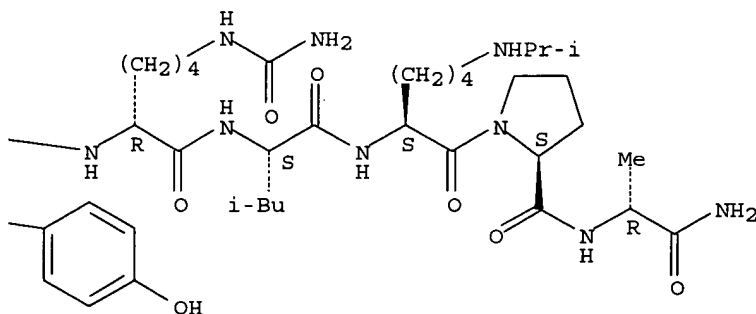
phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-
D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=> d bib abs hitstr l14 tot

L14 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:353144 HCAPLUS

DN 140:368700

TI Methods using exemestane, alone or with other therapeutic agents, for treating estrogen-dependent disorders

IN Wajszczuk, Charles Paul; Gans, Hendrik J. Dekoning; Di Salle, Enrico; Piscitelli, Gabriella; Massimini, Giorgio; Purandare, Dinesh

PA USA

SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of WO 2002 72,106.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004082557	A1	20040429	US 2003-611653	20030702 <--
	WO 2002072106	A2	20020919	WO 2002-EP638	20020118 <--
	WO 2002072106	A3	20031030		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-770911 B2 20010126 <--
 WO 2002-EP638 A2 20020118
 US 2002-393320P P 20020702

AB The invention discloses a method of preventing and/or treating estrogen-dependent disorders selected from endometriosis, uterine fibroids, dysfunctional uterine bleeding, endometrial hyperplasia, polycystic ovarian disease, fibrocystic breast disease and fibrocystic mastopathy, which comprises administering to a female mammal in need of such treatment an effective amount of aromatase inactivator exemestane, alone or in combination with addnl. therapeutic agents. The invention also discloses a method for treating infertility in a female mammal in need of the infertility treatment, comprising administering an effective amount of exemestane to the mammal.

IT 144743-92-0, **Teverelix**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

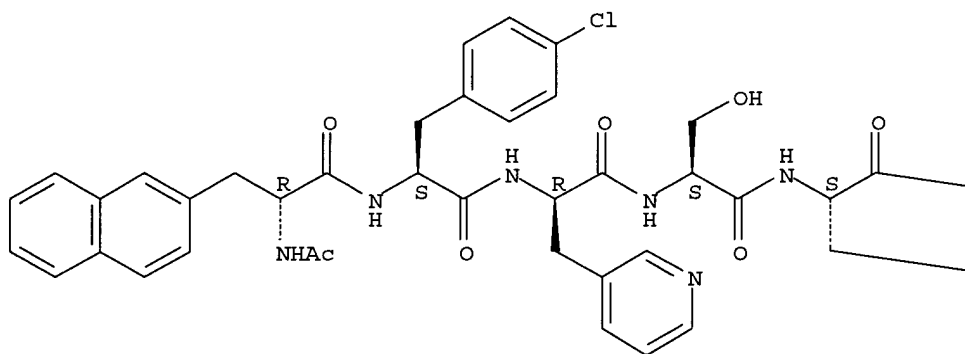
(exemestane, alone or with other therapeutic agents, for treating estrogen-dependent disorders)

RN 144743-92-0 HCAPLUS

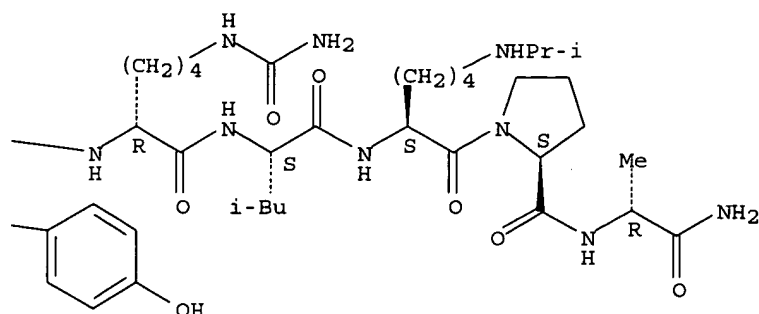
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:414078 HCAPLUS

DN 139:12254

TI Injectable solution of an LHRH antagonist

IN Sarlikiotis, Werner; Bauer, Horst; Rischer, Matthias; Engel, Jurgen

PA Germany

SO U.S. Pat. Appl. Publ., 3 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003100509	A1	20030529	US 2002-279625	20021023 <--
	CA 2412759	AA	20030527	CA 2002-2412759	20021126 <--
PRAI	US 2001-333662P	P	20011127	<--	

AB An aqueous injectable solution of an LHRH antagonist, such as Cetrorelix, in an organic, pharmaceutically acceptable acid, such as gluconic acid is described. A composition contained cetrorelix 500 mg, Tween 80 2 g, δ -gluconolactone 2.4 g, and mannitol 95 g.

IT 144743-92-0, Teverelix

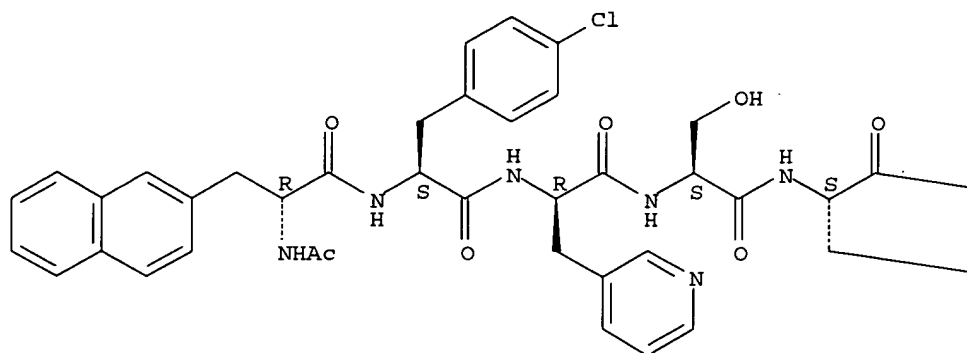
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(injectable solution of an LHRH antagonist)

RN 144743-92-0 HCAPLUS

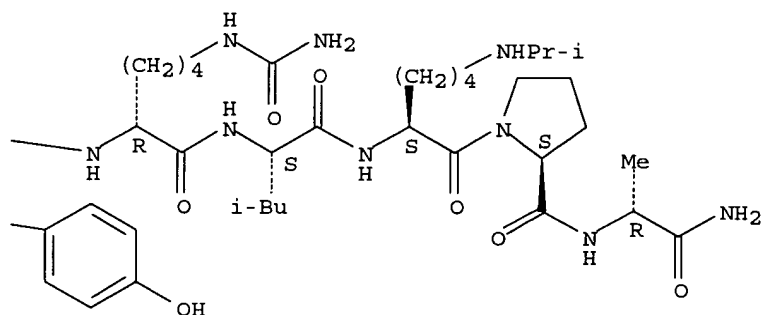
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:907162 HCAPLUS
 DN 137:380043
 TI Treatment of dementia and neurodegenerative diseases with intermediate
 doses of LHRH antagonists
 IN Engel, Jorgen; Voegeli, Rainer
 PA Germany
 SO U.S. Pat. Appl. Publ., 3 pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002177556	A1	20021128	US 2002-133967	20020427 <--
	CA 2444876	AA	20021227	CA 2002-2444876	20020427 <--
	WO 2002102401	A1	20021227	WO 2002-EP4677	20020427 <--
	W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	EP 1392348	A1	20040303	EP 2002-735312	20020427 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
	BR 2002009290	A	20040713	BR 2002-9290	20020427 <--

JP 2004529207 T2 20040924 JP 2003-504987 20020427 <--
 ZA 2003005326 A 20030730 ZA 2003-5326 20030710 <--
 NO 2003004322 A 20030926 NO 2003-4322 20030926 <--
 BG 108339 A 20041130 BG 2003-108339 20031110 <--
 PRAI US 2001-287434P P 20010430 <--
 WO 2002-EP4677 W 20020427

AB The present invention relates to the treatment of dementia and neurodegenerative diseases like Alzheimer's disease with intermediate doses of LHRH antagonists which do not cause a castration. A preferred LHRH antagonist is cetrorelix.

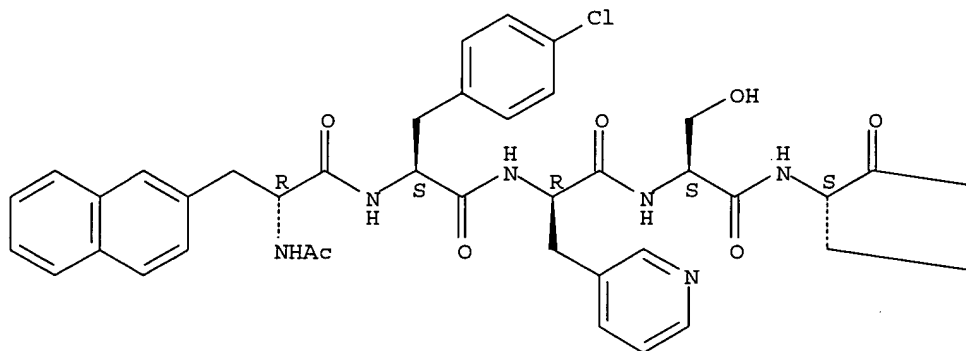
IT 144743-92-0, Teverelix
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (LHRH antagonist; treatment of dementia and neurodegenerative diseases with intermediate doses of LHRH antagonists)

RN 144743-92-0 HCAPLUS

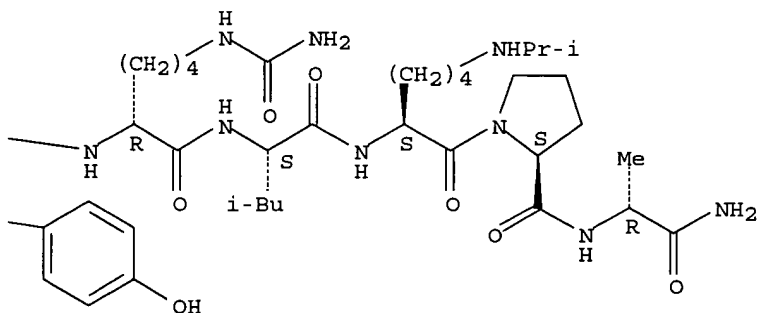
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:716096 HCAPLUS
 DN 137:226651
 TI Combined method for treating hormone-dependent disorders with aromatase

inactivator exemestane and other therapeutic agents

IN Di Salle, Enrico; Piscitelli, Gabriella; Massimini, Giorgio; Purandare, Dinesh; Dekoning, Gans Hendrik

PA Pharmacia Italia S.p.A., Italy; Pharmacia & Upjohn Company

SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DT Patent

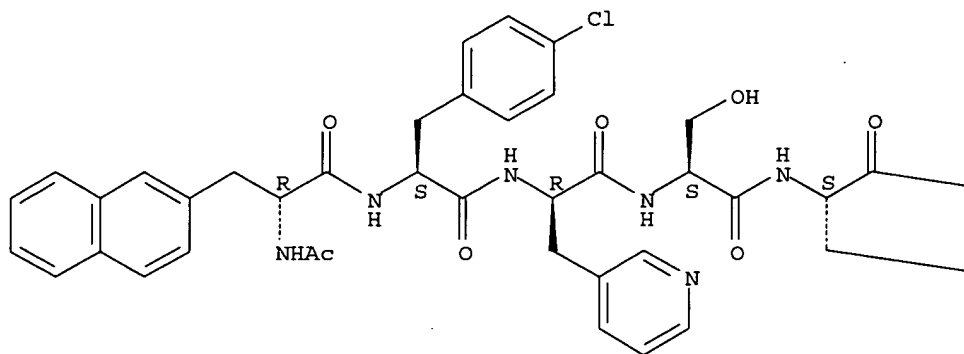
LA English

FAN.CNT 3

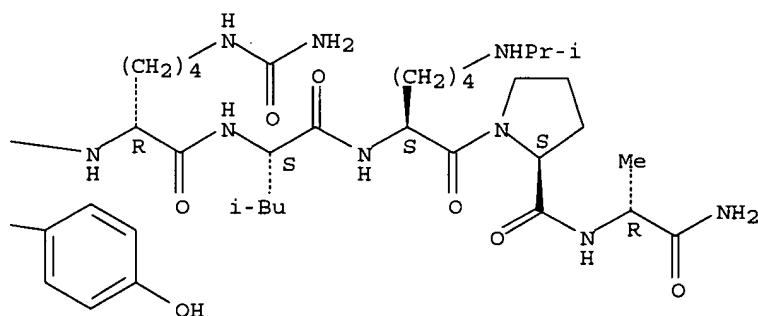
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002072106	A2	20020919	WO 2002-EP638	20020118 <--
	WO 2002072106	A3	20031030		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2434611	AA	20020919	CA 2002-2434611	20020118 <--
	EP 1377298	A2	20040107	EP 2002-727314	20020118 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2004519490	T2	20040702	JP 2002-571065	20020118 <--
	US 2004082557	A1	20040429	US 2003-611653	20030702 <--
PRAI	US 2001-770911	A	20010126	<--	
	WO 2002-EP638	W	20020118		
	US 2002-393320P	P	20020702		
AB	A method of preventing and treating estrogen dependent disorders selected from endometriosis, uterine fibroids, dysfunctional uterine bleeding, endometrial hyperplasia, polycystic ovarian disease, fibrocystic breast disease and fibrocystic mastopathy, is disclosed which is comprised of administering to a mammalian patient in need of such treatment an effective amount of aromatase inactivator exemestane, alone or in combination with addnl. therapeutic agents.				
IT	144743-92-0, Teverelix RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combined method for treating hormone-dependent disorders with aromatase inactivator exemestane and other therapeutic agents)				
RN	144743-92-0 HCAPLUS				
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:521462 HCAPLUS

DN 137:88442

TI Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms

IN Shanahan-Pendergast, Elisabeth

PA Ire.

SO PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002053138	A2	20020711	WO 2002-IE1	20020102 <--
	WO 2002053138	A3	20020919		
	W:	AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG			
	EP 1351678	A2	20031015	EP 2002-727007	20020102 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	US 2004092583	A1	20040513	US 2004-250535	20040102 <--
PRAI	IE 2001-2	A	20010102	<--	
	WO 2002-IE1	W	20020102		

OS MARPAT 137:88442

AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

IT 151272-78-5, Antarelix

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

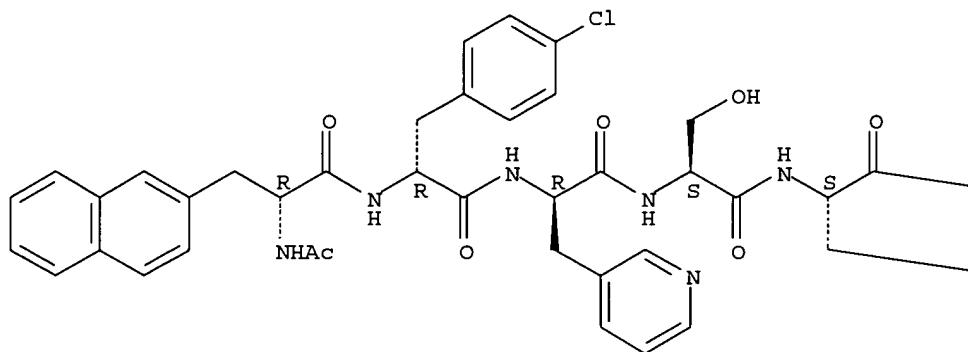
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

RN 151272-78-5 HCAPLUS

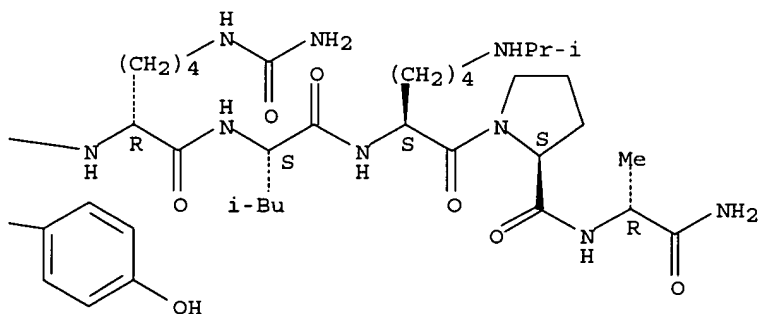
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:391511 HCAPLUS

DN 136:406856

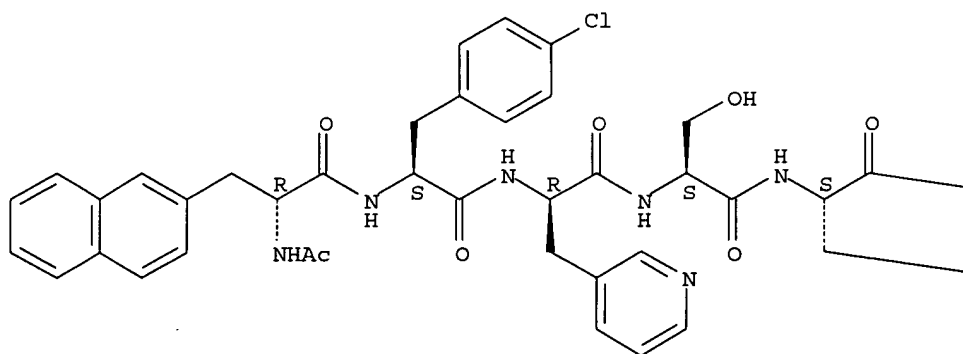
TI Combined therapy against tumors comprising estramustine phosphate and LHRH agonists or antagonists

IN Buchalter, Jeffrey H.; Horak, Ivan D.
 PA Pharmacia & Upjohn Company, USA
 SO PCT Int. Appl., 11 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

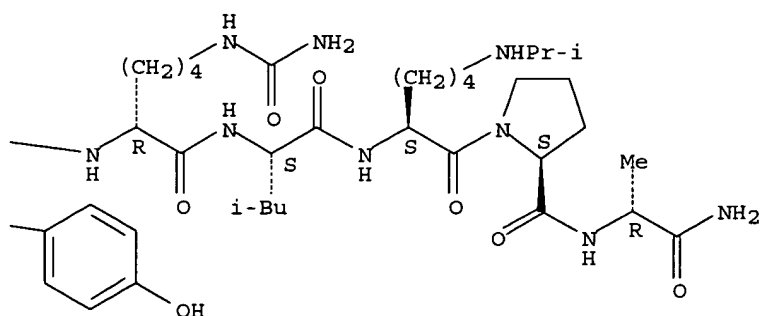
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002039996	A2	20020523	WO 2001-US44161	20011106 <--
	WO 2002039996	A3	20030320		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002028648	A5	20020527	AU 2002-28648	20011106 <--
PRAI	US 2000-714606	A1	20001116	<--	
	WO 2001-US44161	W	20011106	<--	
AB	A method for treating tumors in a mammal, including humans, in need of such a treatment including administering simultaneously, sep. or sequentially to said mammal estramustine phosphate and a LHRH agonist or antagonist, in amts. sufficient to achieve a therapeutically useful effect. Estramustine phosphate arginine salt formulation for injection was prepared				
IT	144743-92-0, Teverelix RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combined therapy against tumors comprising estramustine phosphate and LHRH agonists or antagonists)				
RN	144743-92-0 HCAPLUS				
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L- phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)- D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:391510 HCAPLUS

DN 136:380114

TI Aromatase inhibitor combination with inhibition of testicular and ovarian hormone output for treatment of estrogen-dependent cancers

IN Purandare, Dinesh

PA Pharmacia & Upjohn Company, USA

SO PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002039995	A2	20020523	WO 2001-US43847	20011106 <--
	WO 2002039995	C2	20030206		
	WO 2002039995	A3	20030501		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,				
	HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,				
	LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,				
	PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,				
	US, UZ, VN, YU, ZA, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,				
	KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,				
	IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,				
	GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2428249	AA	20020523	CA 2001-2428249	20011106 <--
	AU 2002030464	A5	20020527	AU 2002-30464	20011106 <--
	EP 1341549	A2	20030910	EP 2001-990699	20011106 <--
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CN 1498112	A	20040519	CN 2001-818938	20011106 <--
	JP 2004536022	T2	20041202	JP 2002-542370	20011106 <--
	ZA 2003003669	A	20040513	ZA 2003-3669	20030513 <--
	NO 2003002206	A	20030715	NO 2003-2206	20030515 <--
	US 2004043938	A1	20040304	US 2003-416844	20030912 <--
PRAI	US 2000-714605	A1	20001116	<--	
	WO 2001-US43847	W	20011106	<--	

AB The invention provides a combination therapy for treating estrogen-dependent cancers in susceptible mammals, including humans, comprising inhibiting testicular or ovarian hormone output and administering at least one aromatase inhibitor.

IT 144743-92-0, Teverelix

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

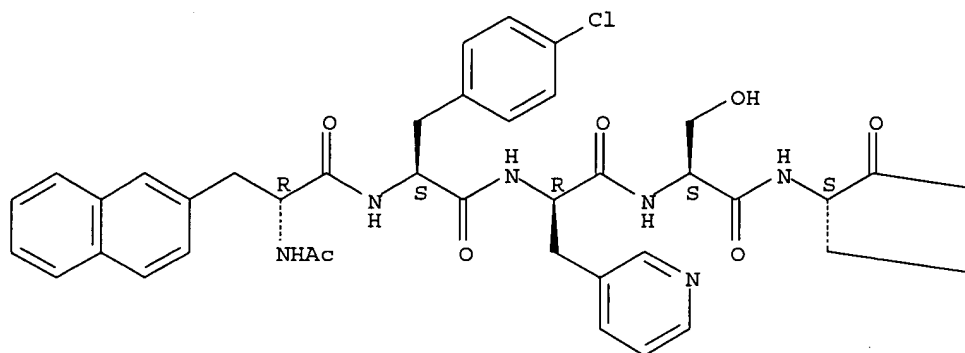
(aromatase inhibitor combination with inhibition of testicular and ovarian hormone output for treatment of estrogen-dependent cancers)

RN 144743-92-0 HCAPLUS

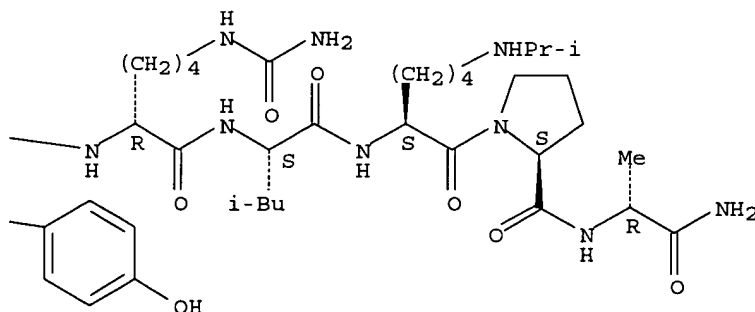
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:171654 HCAPLUS

DN 136:221718

TI Solid peptide preparations for inhalation and their production

IN Lizio, Rosario; Damm, Michael; Sarlikiotis, Werner; Wolf-Heuss, Elisabeth

PA Sofotec GmbH & Co. Kg, Germany

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002017882	A1	20020307	WO 2001-EP9538	20010818 <--
	W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

DE 10043509	A1	20020314	DE 2000-10043509	20000901 <--
AU 2001095483	A5	20020313	AU 2001-95483	20010818 <--
EP 1313452	A1	20030528	EP 2001-976109	20010818 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
CA 2356786	AA	20020301	CA 2001-2356786	20010831 <--
US 2002122826	A1	20020905	US 2001-944060	20010831 <--
US 2005014677	A1	20050120	US 2004-808239	20040323 <--
PRAI DE 2000-10043509	A	20000901	<--	
WO 2001-EP9538	W	20010818	<--	
US 2001-944060	B1	20010831	<--	

AB The invention relates to solid peptide preps., particularly for the inhalation to mammals, to their production, and to their use, for example, in powder inhalators. Drug substances are ground at low temperature in inert solvents; the solvents are removed after the procedure. Solvents are hydrocarbons, and fluorinated hydrocarbons. Thus cetorelixacetate was ground in HFA 227 at -60°C using a double-walled bead mill; the solvent was evaporated; the average particle diameter was 2.5 µm; the peptide impurities increased by 0.08%; and 96 µg/g zircon oxide abrasion from the beads were found. The cetorelixacetate powder (1.03 g) was suspended in 200 g liquid TG227 at -50°C and added to a suspension of 8.96 g SpheroLac 100 in 50 g HFA227. The solvent was evaporated from the mixture; the free-flowing cetorelixacetate-lactose mixture was filled in MDPI cartridges.

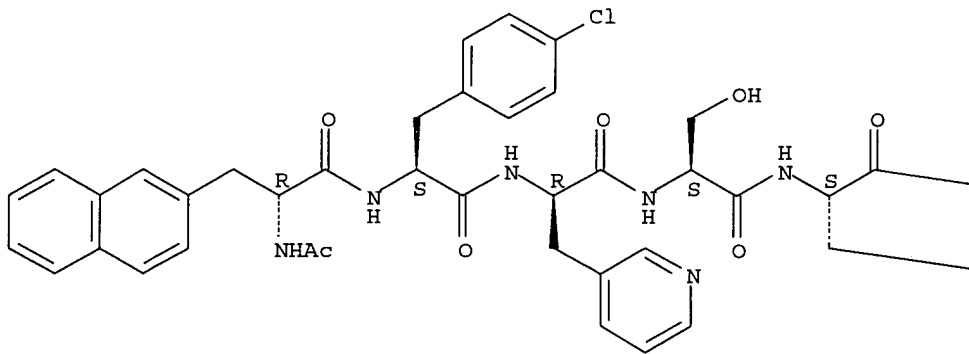
IT 144743-92-0, **Teverelix**
 RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (solid peptide preps. for inhalation and production)

RN 144743-92-0 HCAPLUS

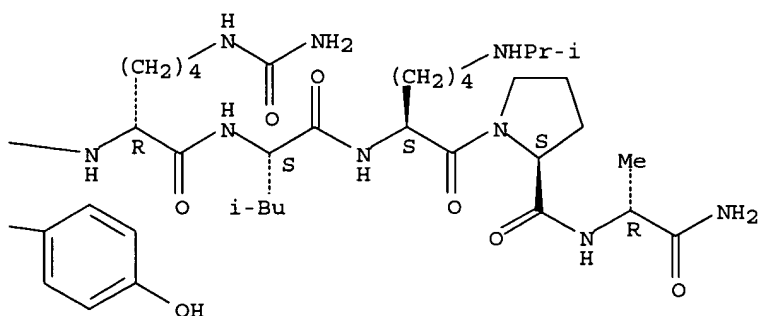
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:31283 HCAPLUS
DN 136:107510
TI Medicinal preparations for treating sex hormone-dependent diseases
IN Igari, Yasutaka; Kamei, Shigeru
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002002144	A1	20020110	WO 2001-JP5808	20010704 <--	
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	AU 2001069439	A5	20020114	AU 2001-69439	20010704 <--	
	JP 2002080397	A2	20020319	JP 2001-203722	20010704 <--	
	CA 2412899	AA	20021212	CA 2001-2412899	20010704 <--	
	EP 1297850	A1	20030402	EP 2001-947821	20010704 <--	
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
	US 2003176360	A1	20030918	US 2003-312998	20030102 <--	
PRAI	JP 2000-208253	A	20000705	<--		
	WO 2001-JP5808	W	20010704	<--		

OS MARPAT 136:107510

AB Disclosed are medicinal preps. for treating sex hormone-dependent diseases which comprise a combination of a compound having a LH-releasing hormone effect or its salt with a compound having a LH-releasing hormone antagonism or its salt for administering the compound having a LH-releasing hormone effect or its salt followed by the compound having a LH-releasing hormone antagonism or its salt. By using these preps., the concentration of a sex hormone (for example, testosterone, LH, FSH, estrogen) can be quickly recovered after the medicable period of a compound having a LH-releasing hormone antagonism or its salt or a preparation containing the same (preferably a sustained-release preparation), which makes it possible to definitely determine the drug rest period in an intermittent treatment. A sustained-release

microcapsule containing LHRH antagonist N-acetyl-D-3-(2-naphthyl)alanyl-D-3-(4-chlorophenyl)alanyl-D-3-(3-pyridyl)alanyl-Ser-N-methyltyrosyl-D-(ε-N-nicotinoyl)lysyl-Leu-(ε-N-isopropyl)lysyl-Pro-D-Ala-NH₂ acetate was prepared, and administered to a rat 4 wk after administration of a LHRH agonist Leuplin to examine the blood concentration of testosterone.

IT 151272-78-5, Antarelix

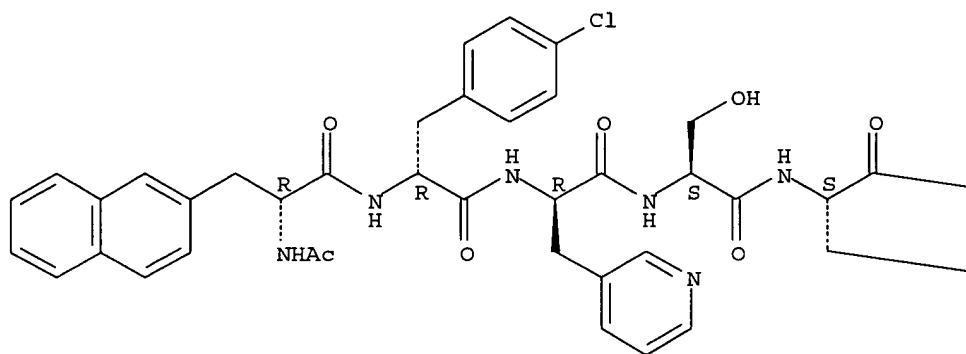
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of LHRH agonists and antagonists for intermittent treatment of sex hormone-dependent diseases)

RN 151272-78-5 HCAPLUS

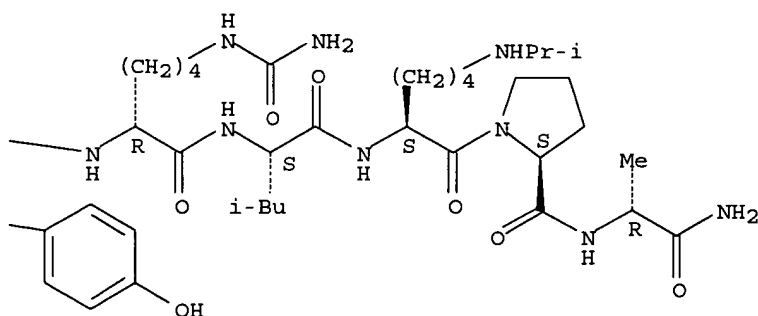
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:862490 HCAPLUS

DN 136:210718

TI Structure-Function Studies of Linear and Cyclized Peptide Antagonists of the GnRH Receptor

AU Beckers, Thomas; Bernd, Michael; Kutscher, Bernd; Kuehne, Ronald; Hoffmann, Silke; Reissmann, Thomas

CS Department of Cancer Research, ASTA Medica AG, Frankfurt/Main, 60314, Germany

SO Biochemical and Biophysical Research Communications (2001), 289(3), 653-663
CODEN: BBRC9; ISSN: 0006-291X

PB Academic Press

DT Journal

LA English

AB Structurally new analogs of the peptidic GnRH receptor antagonist Cetrorelix as well as conformationally constrained cyclized deca- or pentapeptides were synthesized and selected peptides evaluated comprehensively. To understand how structural variations of the antagonistic peptide effect pharmacodynamic properties, binding affinities and antagonistic potencies toward the human and rat GnRH receptor were determined. Whereas large substituents in position 6 of linear peptides are compatible with high binding affinity ($KD < 0.5$ nM), all cyclized peptides except the cyclo[3-10] analog D-52391 depicted low binding affinity ($KD > 10$ nM). Binding affinity and antagonistic potency in vitro correlated for all peptides and surprisingly no discrimination between human and rat receptor proteins was observed. Since receptor residues W101 and N102 are involved in agonist and antagonist binding, equally potent but structurally different antagonists were tested for binding to the resp. W101A and N102A mutants. In contrast to linear decapeptides, residues N102 and W101 are not involved in binding of D-23938 and W101 is the critical residue for D-52391 binding. We conclude that although equally potent, peptidic GnRH receptor antagonists do have distinct interactions within the ligand binding pocket. Finally, selected antagonists were tested for testosterone suppression in male rats. The duration of testosterone suppression below castration levels differed largely from 1 day for Ganirelix to 27 days for D-23487. Systemic availability became evident as the most important parameter for in vivo efficacy. (c) 2001 Academic Press.

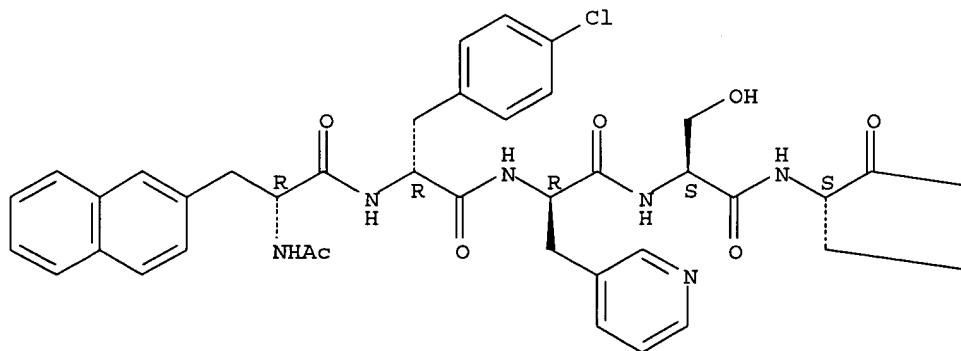
IT 151272-78-5, D 23234
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(structure-function studies of linear and cyclized peptide antagonists of GnRH receptor)

RN 151272-78-5 HCAPLUS

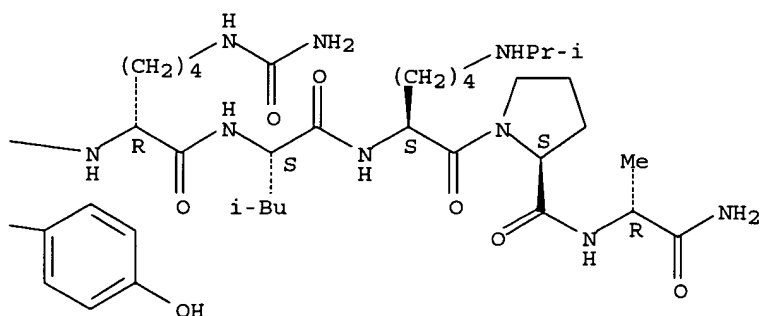
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:799566 HCAPLUS

DN 136:64397

TI The effect of a GnRH antagonist on endocrine and seminal parameters in stallions

AU Hinojosa, A. M.; Bloeser, J. R.; Thomson, S. R. M.; Watson, E. D.

CS Department of Veterinary Clinical Studies, University of Edinburgh, Midlothian, EH25 9RG, UK

SO Theriogenology (2001), 56(5), 903-912

CODEN: THGNBO; ISSN: 0093-691X

PB Elsevier Science Inc.

DT Journal

LA English

AB Relatively little is known about endocrine control of reproduction in the stallion, but gonadotropins are thought to be central in regulating spermatogenesis and libido. The ability to effectively antagonize GnRH, and thereby gonadotropins, is therefore important both in further investigations of hormonal control of reproduction in stallions, and for clin. applications. In the present study four pony stallions were treated with a potent GnRH antagonist, Antarelix. Their libido, seminal parameters, and hormonal profiles were compared with those recorded before administration of the antagonist. Plasma concns. of gonadotropins, testosterone and estradiol decreased by 48 h after antagonist administration, with estradiol and FSH being most consistently suppressed, and remained at reduced concns. for 4 wk. Spermatozoal motility, nos. and morphol. were not significantly affected by treatment, but increasing nos. of round spermatogenic cells were seen in the ejaculate as the trial progressed. Libido was assessed by the time taken for the stallions to regain an erection in the presence of a mare after ejaculation (refractory period). The refractory period increased significantly after treatment. When the stallions were castrated 8 wk after antagonist treatment, histol. evidence of testicular degeneration was present. The authors concluded that use of this antagonist showed promise as a valuable research tool in modulating changes in circulating hormone concns. in stallions. Reversibility of the effects on libido and testicular changes need further investigation.

IT 151272-78-5, Antarelix

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GnRH antagonist effect on endocrine and seminal parameters in pony stallions)

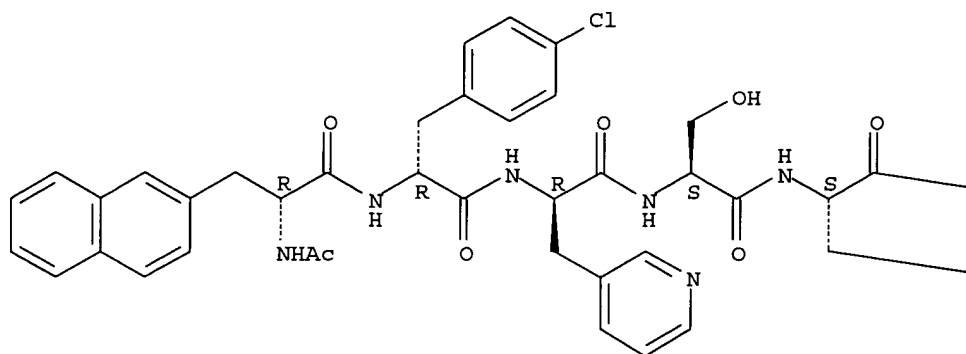
RN 151272-78-5 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX

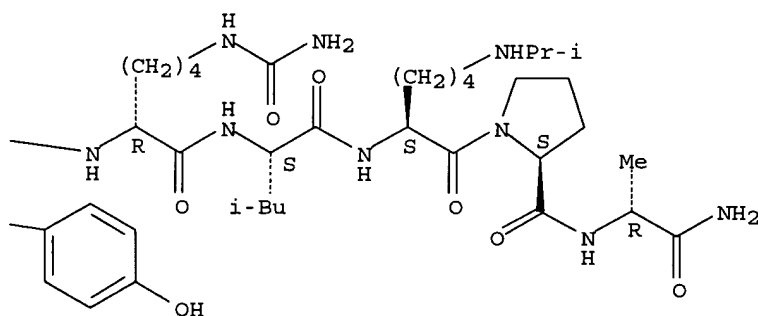
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:334094 HCAPLUS
DN 135:117397
TI Alteration of gonadotrophin and steroid hormone release, and of ovarian function by a GnRH antagonist in gilts
AU Brussow, K.-P.; Schneider, F.; Nurnberg, G.
CS Department of Reproductive Biology, Research Institute for the Biology of Farm Animals, Dummerstorf, 18196, Germany
SO Animal Reproduction Science (2001), 66(1,2), 117-128
CODEN: ANRSDV; ISSN: 0378-4320
PB Elsevier Science B.V.
DT Journal
LA English
AB This study examined the impact of the gonadotrophin-releasing hormone (GnRH) antagonist Antarelix on LH, FSH, ovarian steroid hormone secretion, follicular development and pituitary response to LHRH in cycling gilts. Estrous cycle of 24 Landrace gilts was synchronized with Regumate (for 15 days) followed by 800 IU PMSG 24 h later. In experiment 1, Antarelix (n=6 gilts) was injected i.v. (0.5 mg per injection) twice daily on four consecutive days from day 3 to 6 (day 0=last day of Regumate feeding). Control gilts (n=6) received saline. Blood was sampled daily, and every

20 min for 6 h on days 2, 4, 6, 8 and 10. In experiment 2, gilts (n=12) were assigned to the following treatments: Antarelix; Antarelix +50 µg LHRH on day 4; Antarelix +150 µg LHRH on day 4 or control, 50 µg LHRH only on day 4. Blood samples were collected daily and every 20 min for 6 h on days 2, 4 and 6 to assess LH pulsatility. Ovarian follicular development was evaluated at slaughter. Antarelix suppressed ($P<0.05$) serum LH concns. The amount of LH released on days 4-9 (experiment 1) was 8.80 vs. 36.54 ng ml⁻¹ (S.E.M.=6.54). The pattern of FSH, and the preovulatory estradiol rise was not affected by GnRH antagonist. Suppression of LH resulted in a failure ($P<0.05$) of postovulatory progesterone secretion. Exogenous LHRH (experiment 2) induced a preovulatory-like LH peak, however in Antarelix treated gilts the LH surge started earlier and its duration was less compared to controls ($P<0.01$). Furthermore, the amount of LH released from day 4 to 5 was lower ($P<0.01$) in Antarelix, Antarelix +50 and Antarelix +150 treated animals compared to controls. No differences were estimated in the number of LH pulses between days and treatment. Pulsatile FSH was not affected by treatment. Mean basal LH levels were lower ($P<0.05$) after antagonist treatment compared to controls. Antarelix blocked the preovulatory LH surge and ovulation, but the effects of Antarelix were reduced by exogenous LHRH treatment. The development of follicles larger than 4 mm was suppressed ($P<0.05$) by antagonist treatment. In conclusion, Antarelix treatment during the follicular phase blocked preovulatory LH surge, while FSH and estradiol secretion were not affected. Antarelix failed to alter pulsatile LH and FSH secretor or pituitary responsiveness to LHRH during the preovulatory period.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

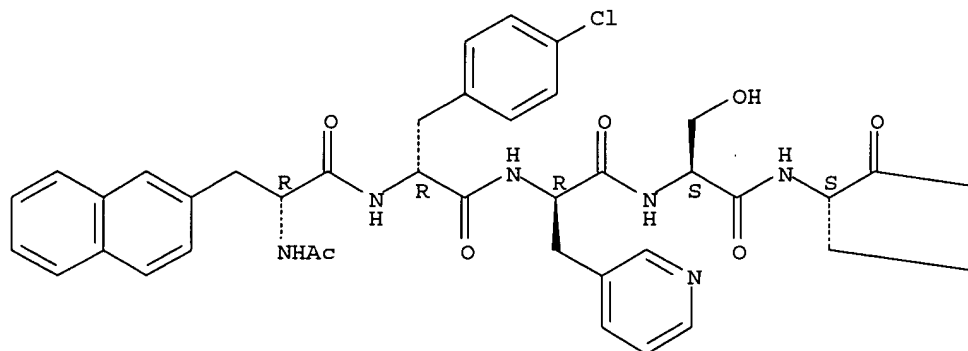
(alteration of gonadotrophin and steroid hormone release, and of ovarian function by a GnRH antagonist in gilts)

RN 151272-78-5 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Chemical structure of a complex molecule, likely a peptide derivative. The structure features a central chain with various side groups, including a 4-hydroxyphenyl group, a 4-aminophenyl group, a 4-aminobenzoyl group, a 4-aminobenzoyl group, a 4-aminobenzoyl group, a 4-aminobenzoyl group, a 4-aminobenzoyl group, a 4-aminobenzoyl group, a 4-aminobenzoyl group, and a 4-aminobenzoyl group. The structure includes stereocenters marked with 'S' and 'i-Bu'.

AB The present invention provides a method for therapeutic management of extrauterine proliferation of endometrial tissue, chronic pelvic pain and fallopian tube obstruction by short term induction treatment with an LH-RH antagonist for 4 to 12 wk. According to another aspect of the present invention, the short term LH-RH treatment is followed by the combined or sep. administration of one or more active agents selected from the group consisting of a contraceptive, preferably an oral contraceptive, a non-steroidal anti-rheumatic agent, an analgetic, an androgen other than a

17- α -alkyl substituted testosterone or any combinations thereof. According to a further aspect of the present invention a pharmaceutical composition comprising an LHRH antagonist and one or more active agents selected from the group consisting of a contraceptive, preferably an oral contraceptive, a non-steroidal anti-rheumatic agent, an analgetic, an androgen other than a 17- α -alkyl substituted testosterone or any combinations thereof are provided.

IT 144743-92-0, **Teverelix**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

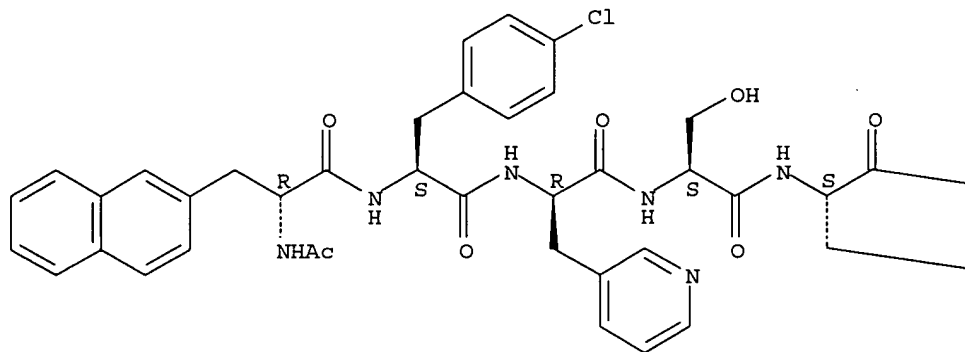
(administration of LH-RH antagonist for therapeutic management of extrauterine proliferation of endometrial tissue, chronic pelvic pain and fallopian tube obstruction)

RN 144743-92-0 HCAPLUS

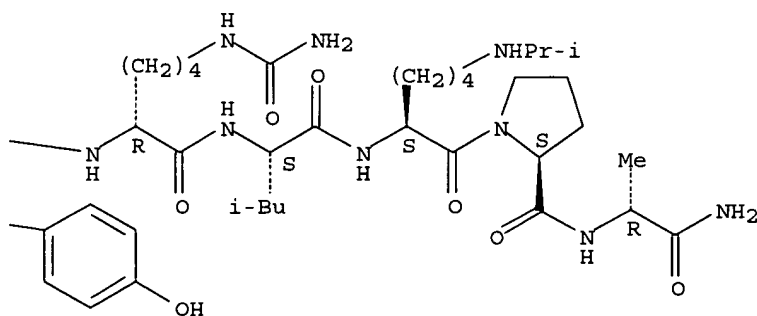
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:61700 HCAPLUS

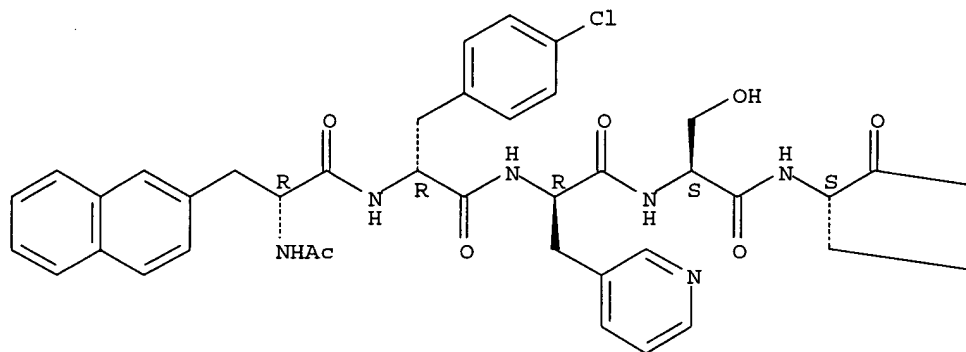
DN 134:305544

TI Stability of several LHRH antagonists against proteolytic enzymes and identification of degradation products by mass spectrometry

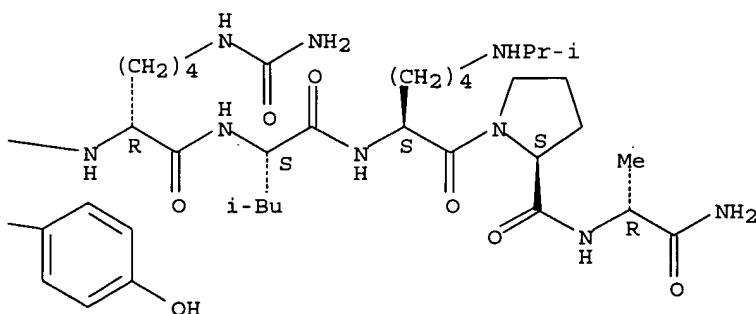
AU Braun, K.; Kuhl, P.; Bernd, M.; Kutscher, B.
 CS Institute of Biochemistry, University of Technology Dresden, Germany
 SO Pharmazie (2001), 56(1), 45-49
 CODEN: PHARAT; ISSN: 0031-7144
 PB Govi-Verlag Pharmazeutischer Verlag
 DT Journal
 LA English
 AB In this study stabilities of several LHRH antagonists against proteolytic enzymes are compared. For the enzymic tests 15 proteases which differ in both substrate specificity and pH optimum were selected. The cyclic and two linear antagonists proved to be extraordinarily stable against the enzymes used over an incubation time of 50 h. Some degradation products were identified by HPLC combined with mass spectrometry.
 IT 151272-78-5, Antarelix
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (LHRH antagonists stability against proteolytic enzymes and identification of degradation products by mass spectrometry)
 RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

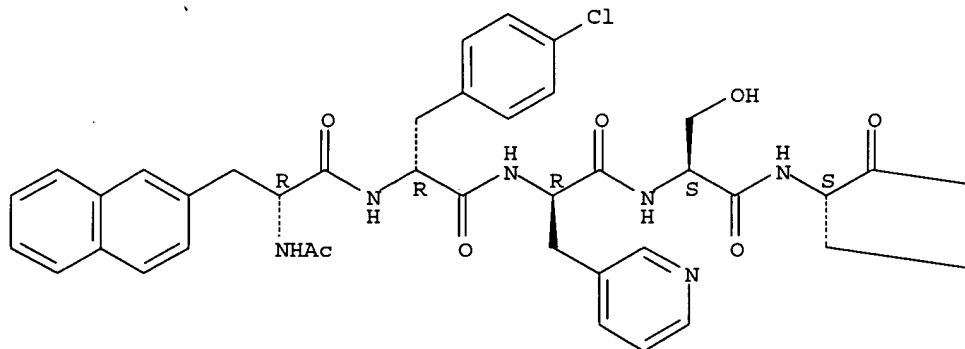
L14 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:863337 HCAPLUS
 DN 134:85570
 TI Diet and the aetiology of temporal advances in human and rodent sexual development
 AU Ashby, J.; Tinwell, H.; Odum, J.; Kimber, I.; Brooks, A. N.; Pate, I.; Boyle, C. C.
 CS Zeneca Central Toxicology Laboratory, Macclesfield, SK10 4TJ, UK
 SO Journal of Applied Toxicology (2000), 20(5), 343-347
 CODEN: JJATDK; ISSN: 0260-437X
 PB John Wiley & Sons Ltd.
 DT Journal
 LA English
 AB The authors evaluated the effects of a range of infant formula on the sexual development of rodents. Soy-based formula, a cows' milk formula (SMA Gold), AIN-76Avy diet, and Burgen bread were presented to Alderley Park strain rats in their drinking bottles between postnatal day 21/22 to 24/25. Nonylphenol (NP), diethylstilbestrol (DES), and estradiol (E2) were tested in oral gavage studies. Antarelix (ANT), anastrozole (ANAS), and faslodex (FAS) as puberty inhibitors were employed to characterize the mechanism of sexual development. All formulas showed uterotrophic activity, with the soy-based material consistently giving stronger responses. The uterotrophic activities of Infasoy, SMA Gold, and AIN-76A diet were inhibited by FAS. ANT abolished the uterotrophic activities of soy-based formula, SMA Gold and AIN-76A, but the activity for the exogenous estrogen-receptor agonists, DES, NP and E2, was retained. Infasoy or AIN-76A led to advances in both the mean day of vaginal opening (VO) and first estrus. Mean body weight on the day of individual VO was significantly lower than than for control animals, confirming advances in sexual maturation independent of weight gain. These results indicate that the sexual development of rodents may be advanced either as a direct consequence of exogenous synthetic or dietary estrogens interacting with estrogen receptors of reproductive tissues, or via a centrally mediated increase in endogenous estrogens.

IT 151272-78-5, Antarelix
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (diet and the etiol. of temporal advances in human and rodent sexual development)

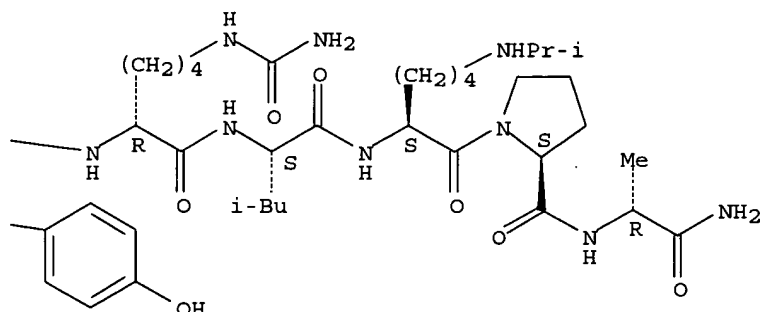
RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:838699 HCAPLUS

DN 134:110702

TI Control of follicular development and luteal function in the mare: Effects of a GnRH antagonist

AU Watson, E. D.; Pedersen, H. G.; Thomson, S. R. M.; Fraser, H. M.

CS Department of Veterinary Clinical Studies, University of Edinburgh, Midlothian, EH25 9RG, UK

SO Theriogenology (2000), 54(4), 599-609

CODEN: THGNBO; ISSN: 0093-691X

PB Elsevier Science Inc.

DT Journal

LA English

AB Control of the equine estrus cycle was studied by suppressing gonadotropin secretion by administration of a GnRH antagonist to cyclic pony mares. Four mares received vehicle (control cycle) or a GnRH antagonist, Antarelix (100 µg/kg) on Day 8 of diestrus, and blood samples were collected at 15-min intervals from 0 to 16 h, 24 to 36 h, and daily until the next ovulation. Ovarian activity was monitored by transrectal ultrasonog., and measurement of plasma concns. of progesterone and estradiol. Antagonist treatment eliminated large diestrus pulses of LH. Progesterone concns. had fallen significantly in all mares by the day after treatment and, in three of the four mares, remained low until luteolysis. However timing of luteolysis (ie., progesterone concns. <1 ng/mL) was not affected by antagonist treatment. The preovulatory surges of estradiol and LH were significantly delayed in the treatment cycle, as was the appearance of a preovulatory follicle >30 mm. Cycle length was significantly longer during the treatment than the control cycle. These results show that treatment of diestrus mares with a GnRH antagonist attenuated progesterone secretion, indicating a role for LH in control of CL function in the mare, and delayed ovulation presumably because of lack of gonadotropic support.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

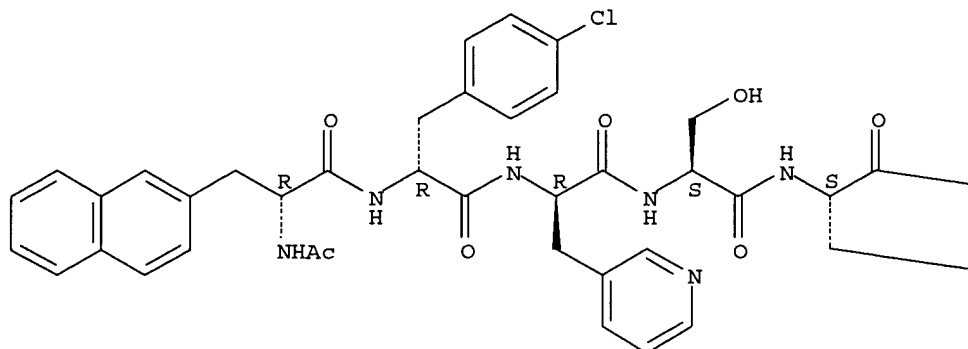
(control of follicular development and luteal function in diestrus mares with GnRH antagonist)

RN 151272-78-5 HCAPLUS

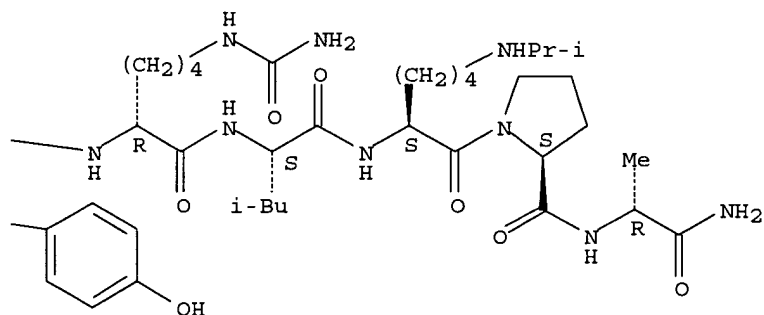
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:725497 HCAPLUS
DN 133:261948
TI Method for a programmed controlled ovarian stimulation protocol
IN Engel, Jurgan; Riethmuller-winzan, Hilde
PA Asta Medica A.-G., Germany
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059542	A1	20001012	WO 2000-EP2466	20000321 <--
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2367214	AA	20001012	CA 2000-2367214	20000321 <--
AU 2000041069	A5	20001023	AU 2000-41069	20000321 <--
AU 768544	B2	20031218		
EP 1165138	A1	20020102	EP 2000-920521	20000321 <--
EP 1165138	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO

BR 2000009477	A	20020108	BR 2000-9477	20000321 <--
JP 2002541122	T2	20021203	JP 2000-609104	20000321 <--
NZ 514964	A	20030829	NZ 2000-514964	20000321 <--
RU 2226395	C2	20040410	RU 2001-129500	20000321 <--
AT 265862	E	20040515	AT 2000-920521	20000321 <--
PT 1165138	T	20040930	PT 2000-920521	20000321 <--
ES 2219331	T3	20041201	ES 2000-920521	20000321 <--
NO 2001004736	A	20011126	NO 2001-4736	20010928 <--
ZA 2001007974	A	20020806	ZA 2001-7974	20010928 <--
BG 106045	A	20020531	BG 2001-106045	20011024 <--
PRAI US 1999-127241P	P	19990331 <--		
US 1999-131632P	P	19990428 <--		
WO 2000-EP2466	W	20000321 <--		

AB A method of therapeutic management of infertility by programming of controlled ovarian stimulation (COS) and assisted reproductive procedures (ART) the improvement consisting of (a) suppression of premature ovulation with an LHRH-antagonist in controlled ovarian stimulation (COS) and assisted reproductive techniques (ART) with multiple follicle and oocyte development; (b) programming the start of controlled ovarian stimulation (COS) by the administration of progestogen only - or alternatively combined oral contraceptive preps.; (c) exogenous stimulation of the ovarian follicle growth; (d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; (e) application of assisted reproduction techniques, especially of IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection.

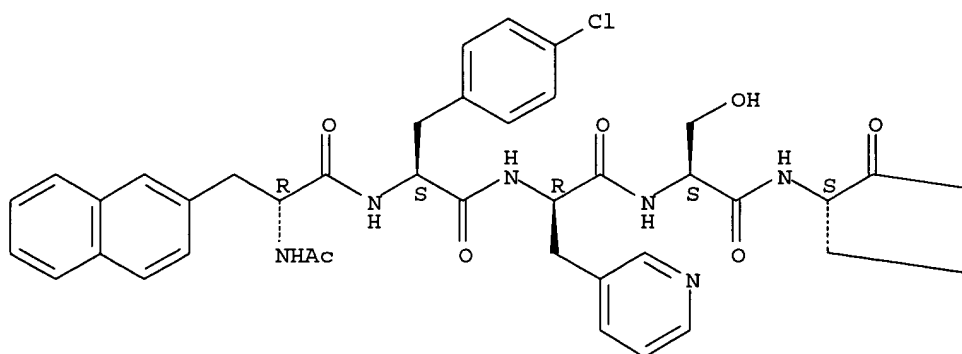
IT 144743-92-0, **Teverelix**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

RN 144743-92-0 HCAPLUS

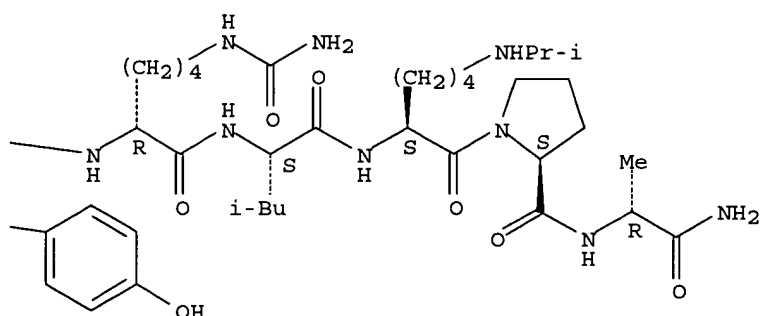
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:573692 HCAPLUS

DN 133:182987

TI Sustained release salts of pharmaceutically active peptides and their production

IN Bauer, Horst; Deger, Wolfgang; Sarlikiotis, Werner; Damm, Michael

PA Asta Medica A.-G., Germany

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047234	A1	20000817	WO 2000-EP697	20000129 <--
	W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2360110	AA	20000817	CA 2000-2360110	20000129 <--
	NZ 513748	A	20010928	NZ 2000-513748	20000129 <--
	BR 2000008786	A	20011106	BR 2000-8786	20000129 <--
	EP 1150717	A1	20011107	EP 2000-906245	20000129 <--
	EP 1150717	B1	20050622		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200102289	T2	20011221	TR 2001-200102289	20000129 <--
	JP 2002536421	T2	20021029	JP 2000-598185	20000129 <--
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	RU 2239457	C2	20041110	RU 2001-125033	20000129 <--
	AT 298252	E	20050715	AT 2000-906245	20000129 <--
	NO 2001003851	A	20010928	NO 2001-3851	20010807 <--
	ZA 2001006467	A	20011219	ZA 2001-6467	20010807 <--
	BG 105864	A	20020430	BG 2001-105864	20010901 <--
PRAI	US 1999-119076P	P	19990208	<--	
	WO 2000-EP697	W	20000129	<--	

AB Substained delivery pharmaceutical compns. comprise a water insol. salt of a pharmaceutically active ionic peptide and a counterionic carrier macromol. The peptide may be an LHRH antagonist such as cetrorelix and the macromol. may be an anionic polysaccharide such as CM-cellulose. The salt is prepared using ion exchangers to sep. remove the counterions from the peptide and the carrier macromol. thereby forming free peptide/macromol. ions. These free peptide and macromol. ions are then

combined to form the water insol. peptide-macromol. salt. A lyophilizate of cetrorelix-CM-cellulose salt was prepared

IT 144743-92-0, Teverelix

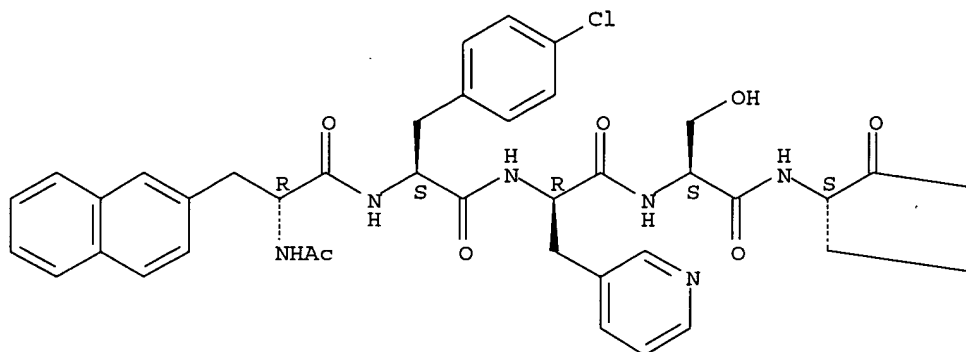
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release salts of pharmaceutically active peptides)

RN 144743-92-0 HCAPLUS

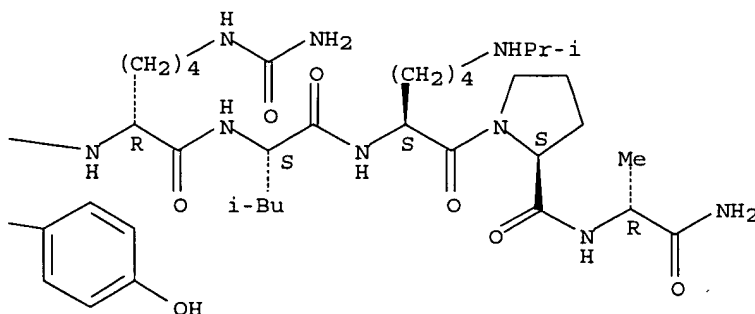
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:510174 HCAPLUS

DN 133:233063

TI Pharmacodynamics and drug action: Pituitary and gonadal endocrine effects and pharmacokinetics of the novel luteinizing hormone-releasing hormone antagonist **teverelix** in healthy men-a first-dose-in-humans study

AU Erb, Katharina; Pechstein, Birgit; Schueler, Armin; Engel, Juergen; Hermann, Robert

CS Department of Human Pharmacology, ASTA Medica AG, Frankfurt am Main, 60314, Germany

SO Clinical Pharmacology & Therapeutics (St. Louis) (2000), 67(6), 660-669

CODEN: CLPTAT; ISSN: 0009-9236

PB Mosby, Inc.

DT Journal

LA English

AB **Teverelix** is a novel synthetic peptidic LH-releasing hormone (LHRH) antagonist. Single s.c. morning doses of **teverelix** acetate (either 0.5, 1, 2, 3, or 5 mg base) were investigated in a randomized, single-blind, placebo-controlled, dose-escalating parallel-group design in healthy men. Six subjects received **teverelix**, and two subjects received placebo per dose level. Blood samples for lutropin, LH, and follitropin, FSH, and testosterone, as well as for pharmacokinetics, were withdrawn up to 120 h after dosing. Serum hormone levels were determined by electrochemoluminescence immunoassays, and plasma **teverelix** concns. were determined by RIA. **Teverelix** led to a rapid, marked suppression of LH, testosterone and, to a lesser extent, FSH. Median maximum suppressions compared with predose levels were -93% for LH and -54% for FSH after **teverelix** 5 mg, and -93% for testosterone after **teverelix** 3 mg, resp. After 5 mg **teverelix**, testosterone suppression <1 ng/mL started a median of 12 h after dosing and lasted for a median of 33 h. The duration of testosterone suppression increased with dose. Geometric means of peak **teverelix** plasma concns. were 4.5 ng/mL (0.5 mg **teverelix**) to 49.0 ng/mL (5 mg **teverelix**) and t_{max} occurred between 1 and 4 h after dosing. Geometric means of the area under the **teverelix** plasma concentration-time course from zero to time of the last quantifiable plasma concentration [AUC(0-t_{last})] were 54.9 ng/h/mL (0.5 mg **teverelix**) to 881.8 ng/h/mL (5 mg **teverelix**). Median values for apparent terminal half-lives ranged from 24 to 75 h. The most frequently reported adverse events were short-lasting mild injection-site reactions. **Teverelix** showed pronounced LH and testosterone suppressive effects after single s.c. doses in healthy men. Duration of hormone suppression increased with dose. **Teverelix** was well tolerated. This profile indicates potential for further clin. use.

IT 144743-92-0, **Teverelix**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

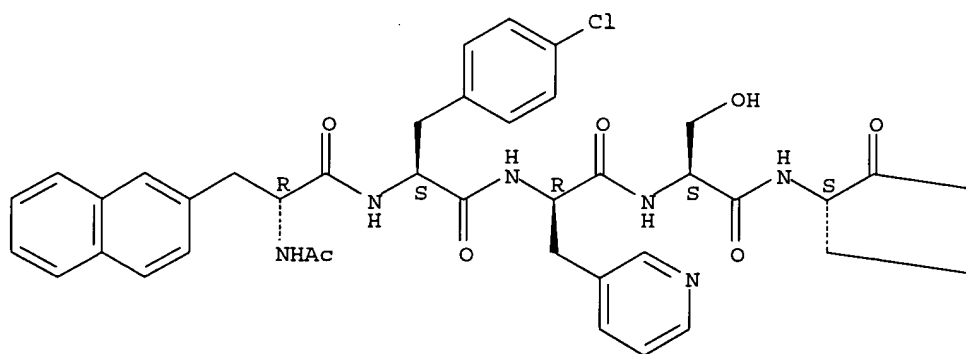
(pituitary and gonadal endocrine effects and pharmacokinetics, safety and tolerability of LH-RH antagonist **Teverelix** in healthy men)

RN 144743-92-0 HCAPLUS

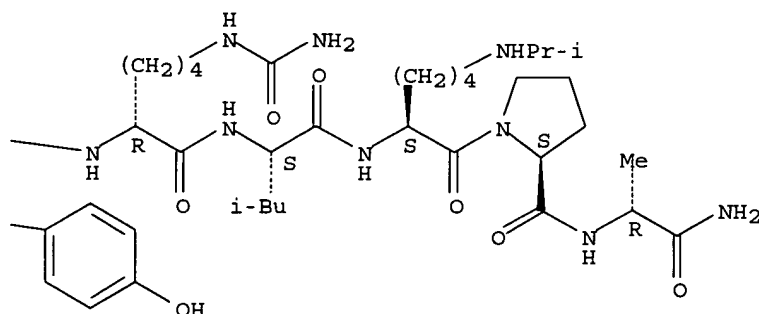
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:97949 HCAPLUS
DN 132:246468
TI Effect of GnRH antagonist-induced prolonged follicular phase on follicular atresia and oocyte developmental competence in vitro in superovulated heifers
AU Oussaid, B.; Lonergan, P.; Khatir, H.; Guler, A.; Monniaux, D.; Touze, J. L.; Beckers, J. F.; Cognie, Y.; Mermillod, P.
CS INRA, Unite Physiologie de la Reproduction des Mammiferes Domestiques, Nouzilly, 37380, Fr.
SO Journal of Reproduction and Fertility (2000), 118(1), 137-144
CODEN: JRPFA4; ISSN: 0022-4251
PB Journals of Reproduction and Fertility Ltd.
DT Journal
LA English
AB A GnRH antagonist (Antarelix) was used to suppress endogenous pulsatile secretion of LH and delay the preovulatory LH surge in superovulated heifers to study the effect of a prolonged follicular phase on both follicle and oocyte quality. Estrous cycles were synchronized in 12 heifers with progestagen (norgestomet) implants for 10 days. On day 4 (day 0 = day of estrus), heifers were stimulated with 24 mg FSH for 4 days and luteolysis was induced at day 6 with PGF2 α (2 mL Estrumate). Animals in the control group were killed 24 h after the last FSH injection. At this time, heifers in group A36h and group A60h were treated with 1.6 mg of Antarelix every 12 h for 36 and 60 h, resp., and then killed. After dissection of ovarian follicles, oocytes were collected for individual in vitro maturation, fertilization and culture; follicular fluid was collected for determination of steroid concns., and granulosa cells were smeared, fixed and stained for evaluation of pycnosis rates. Granulosa cell smears showed that 90% of follicles were healthy in the control group. In contrast, 36 and 58% of the follicles in group A36h showed signs of early or advanced atresia, resp., while 90% of the follicles in group A60h showed signs of late atresia. Intrafollicular concns. of estradiol decreased from healthy follicles (799.14 ng/mL) to late atretic follicles (3.96 ng/mL). Progesterone concns. were higher in healthy follicles compared with atretic follicles, irres. of degree of atresia. Estradiol:progesterone ratios decreased from healthy (4.58) to late atretic follicles (0.07). The intrafollicular concns. of estradiol and progesterone were significantly higher in the control than in the treated groups. The estradiol:progesterone ratio was higher in the control (4.55) than in the A36h (0.40) and A60h (0.07) groups.

Unexpectedly, the cleavage rate of fertilized oocytes, blastocyst rate and number of cells per blastocyst were not significantly different among control (85%, 41% and 95), A36h (86%, 56% and 93) and A60h (88%, 58% and 79) groups. In addition, there were no significant differences in the blastocyst rates from oocytes derived from healthy (45%), early atretic (54%), advanced atretic (57%) and late atretic follicles (53%). In conclusion, the maintenance of the preovulatory follicles in superovulated heifers with a GnRH antagonist induced more atresia and a decrease in estradiol and progesterone concns. However, the developmental potential in vitro to day 8 of the oocytes recovered from these atretic follicles was not affected.

IT 151272-78-5, Antarelix

RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)

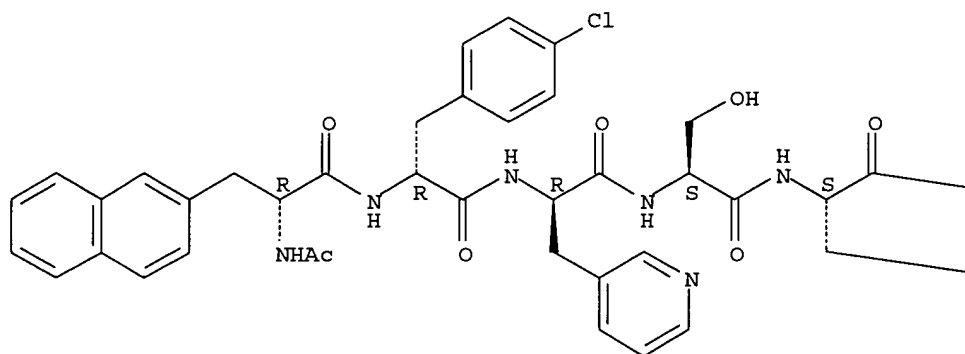
(LH-RH antagonist-induced prolonged follicular phase effect on follicular atresia and oocyte developmental competence in vitro in superovulated heifers)

RN 151272-78-5 HCAPLUS

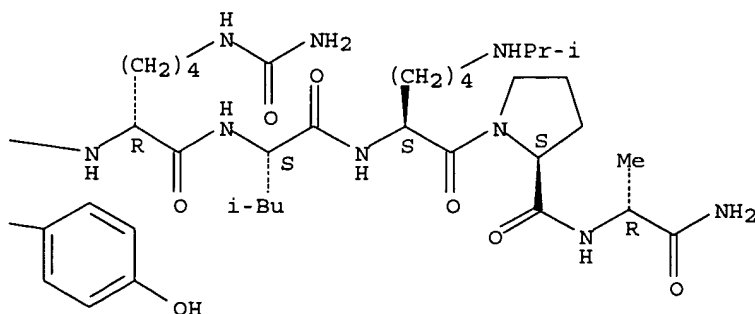
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

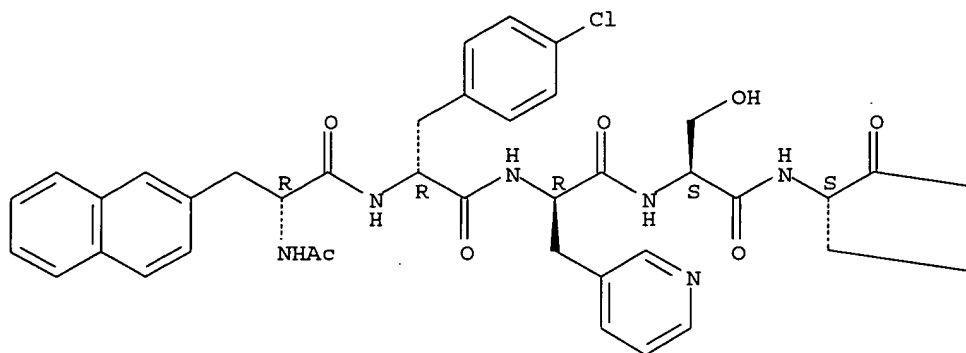


RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

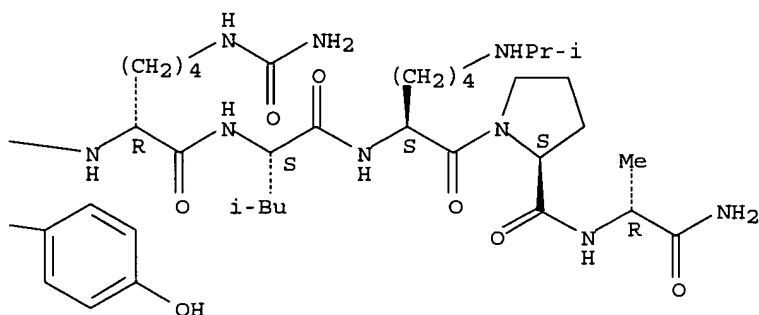
L14 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:97943 HCAPLUS
 DN 132:246466
 TI Effects of the Booroola Fec gene on ovarian follicular populations in superovulated Romanov ewes pretreated with a GnRH antagonist
 AU Dufour, J. J.; Cognie, Y.; Mermillod, P.; Mariana, J-C.; Romain, R. F.
 CS Departement des sciences animales, Faculte des sciences de l'agriculture et de l'alimentation, Sainte-Foy, QC, G1K 7P4, Can.
 SO Journal of Reproduction and Fertility (2000), 118(1), 85-94
 CODEN: JRPFA4; ISSN: 0022-4251
 PB Journals of Reproduction and Fertility Ltd.
 DT Journal
 LA English
 AB Endocrine control of follicular growth was studied in mature Romanov ewes carrying (RF+) or not carrying (R++) the Booroola Fec gene during an estrous cycle after gonadotropin-dependent follicles were suppressed by treatment with an antagonist of GnRH (Antarelix, 0.5 mg per day) and superovulatory treatment was administered. The left ovary was removed after 10 days of treatment (saline or Antarelix) and the right ovary was removed at the end of the superovulatory treatment. Ewes of both genotypes treated with Antarelix had lower plasma LH concns. than did controls from day 0 to day 10. The inhibitory effect of Antarelix on LH concentration increased with day of treatment. The variability in FSH concns. during the initial 10 days was reduced by Antarelix treatment in both genotypes. Plasma FSH concns. were higher in RF+ ewes than in R++ ewes. In both genotypes, FSH concns. varied significantly with day of treatment, with the lowest concns. at day 8 and the highest concns. at day 5. RF+ ewes had a greater total and atretic number of antral follicles 0.62-1.12, 1.12-2.00 and 2.00-3.00 mm in diameter (classes 2, 3 and 4) than did R++ ewes before and after superovulatory treatment. After superovulatory treatment, the total number of atretic and non-atretic follicles > 3.00 mm in diameter (class 5) increased in both genotypes. Superovulatory treatment also increased the number of total and atretic class 4 follicles in RF+ only. Conversely, superovulatory treatment decreased the mean number of class 3 follicles in both genotypes, while the number of atretic follicles was decreased only in R++ ewes. Antarelix treatment significantly reduced the percentage of follicles > 2.00 mm in diameter in RF+ but not in R++ ewes. Antarelix treatment before superovulatory treatment increased the total number of class 4 follicles in both genotypes but the increase was more significant in RF+ than in R++ ewes. These results indicate that Antarelix pretreatment favors a greater superovulatory response in Romanov ewes carrying the Fec gene because ovulatory follicles are recruited from a wider range of follicular size classes.
 IT 151272-78-5, Antarelix
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (superovulatory effect of GnRH antagonist antarelix in Booroola Fec gene pos. vs. neg. Romanov ewes)
 RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:84613 HCAPLUS

DN 132:141952

TI Bioimplant formulations containing stearin

IN Trigg, Timothy Elliot; Walsh, John Desmond; Rathjen, Deborah Ann

PA Peptech Limited, Australia

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004897	A1	20000203	WO 1999-AU585	19990720 <--
	W:				
	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,				
	DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,				
	JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,				
	MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,				
	TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,				
	MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				
	ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				
	CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2336879	AA	20000203	CA 1999-2336879	19990720 <--

AU 9948890	A1	20000214	AU 1999-48890	19990720 <--
AU 755443	B2	20021212		
BR 9912275	A	20010417	BR 1999-12275	19990720 <--
EP 1104296	A1	20010606	EP 1999-932545	19990720 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002521331	T2	20020716	JP 2000-560890	19990720 <--
US 6913761	B1	20050705	US 2001-743059	19990720 <--
ZA 2001000567	A	20020121	ZA 2001-567	20010119 <--
PRAI AU 1998-4730	A	19980720	<--	
AU 1998-4731	A	19980720	<--	
AU 1999-324	A	19990513	<--	
WO 1999-AU585	W	19990720	<--	

AB A pharmaceutical and/or veterinary formulation comprising about 2-30 % (weight/weight) of at least 1 active agent, about 0.5-20.0% of a pore-forming agent and the balance stearin. Such formulations provide sustained release of the at least one active agent in humans and other animals for periods of 7 days up to about 2 yr. Stearin and lecithin were mixed with freeze-dried deslorelin. The mixed material was extruded by using a ram extruder and was equilibrated at 55°. The product was then extruded at a rate of 3 g over a 30-s period and cooled and the the long rods produced were sectioned into lengths of the required weight. In dissoln. tests, after an initial rapid release of deslorelin, a sustained release extending over a prolonged period (110 days) was achieved. The average daily rate of deslorelin release during the sustained release period was within the range 50-2 µg/day.

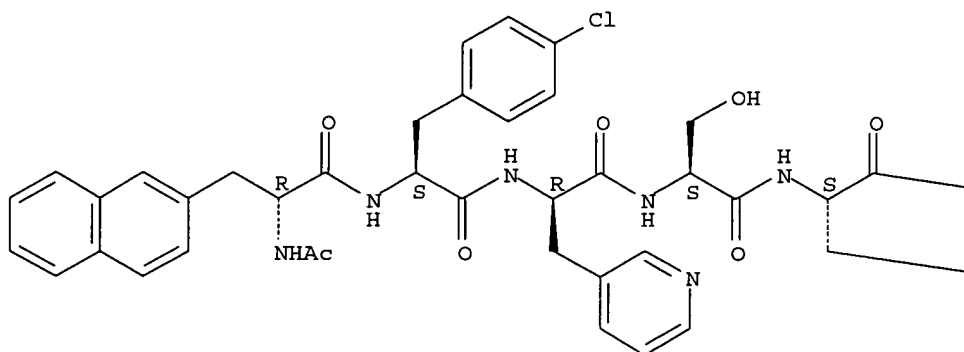
IT 144743-92-0, **Teverelix**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (bioimplant formulations containing stearin)

RN 144743-92-0 HCAPLUS

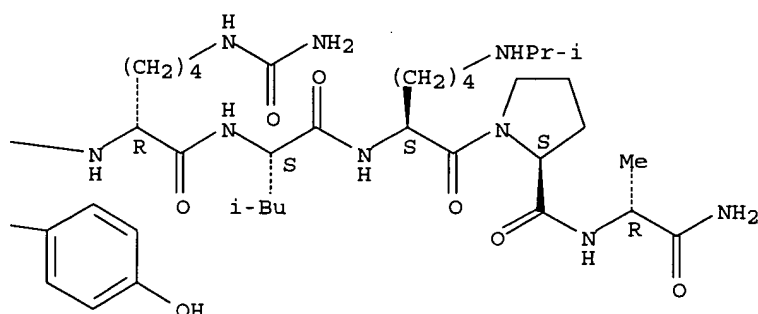
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:768433 HCAPLUS

DN 132:73838

TI Luteal regression in the primate: different forms of cell death during natural and gonadotropin-releasing hormone antagonist or prostaglandin analogue-induced luteolysis

AU Fraser, H. M.; Lunn, S. F.; Harrison, D. J.; Kerr, J. B.

CS MRC Reproductive Biology Unit, Edinburgh, EH3 9ET, UK

SO Biology of Reproduction (1999), 61(6), 1468-1479

CODEN: BIREBV; ISSN: 0006-3363

PB Society for the Study of Reproduction

DT Journal

LA English

AB Morphol. changes in the corpus luteum following natural and induced luteolysis in the marmoset were investigated by light and electron microscopy. Functional corpora lutea were studied in the mid and late luteal phase, naturally regressed corpora lutea in the early and late follicular phase, and corpora lutea induced to regress by administration of GnRH antagonist or prostaglandin F2 α analog in the midluteal phase. Natural luteolysis was associated with lutein cell atrophy, condensation of cytoplasmic inclusions and organelles, and accumulation of lipid. GnRH antagonist treatment resulted in aggregations of smooth membranes and myelin-like bodies in the cytoplasm of the lutein cells together with complex aggregations of degenerative cells. After prostaglandin treatment, the lutein cells contained numerous small and large vesicles; as the degenerative changes advanced, these vesicles coalesced into alveolar-type vacuoles, and nuclei involuted. These results show that in the marmoset, natural luteolysis and the two luteolytic treatments reveal different forms of luteal degeneration and cell death, none of which fit the ultrastructural criteria for apoptosis. More emphasis needs to be placed on understanding these predominant nonapoptotic forms of cell death in order to elucidate the process of luteolysis in the primate.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(marmoset corpus luteum morphol. and different forms of cell death during natural and LH-RH antagonist or prostaglandin analog-induced luteolysis)

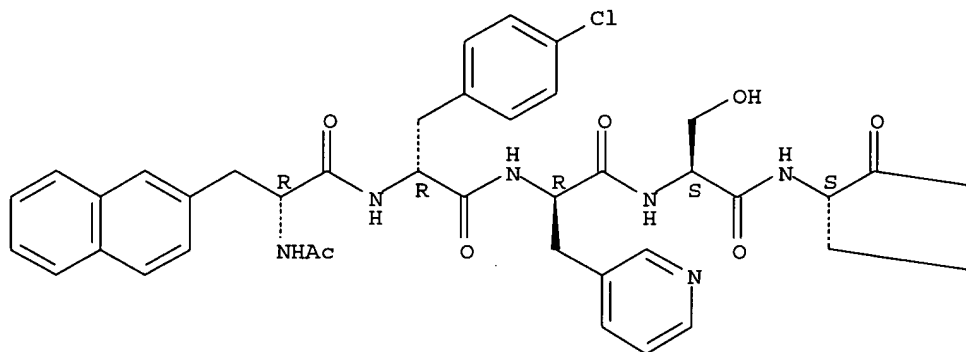
RN 151272-78-5 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX

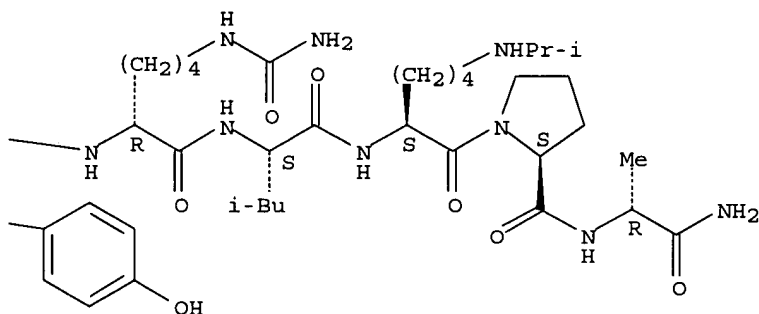
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:708625 HCAPLUS

DN 131:295922

TI Method for the treatment of fertility disorders using an LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination

IN Engel, Jurgun; Riethmuller-Winzen, Hilde; Reissmann, Thomas

PA Asta Medica Aktiengesellschaft, Germany

SO PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DT Patent

LA English

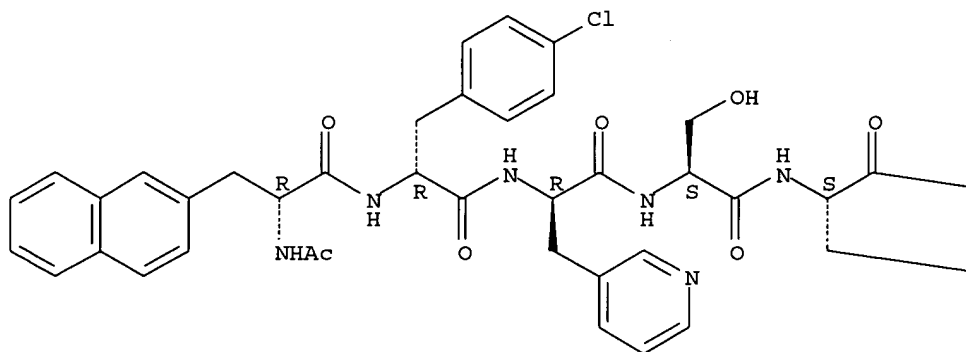
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9955357	A1	19991104	WO 1999-EP2133	19990329 <--	
	W:			AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:			AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE		

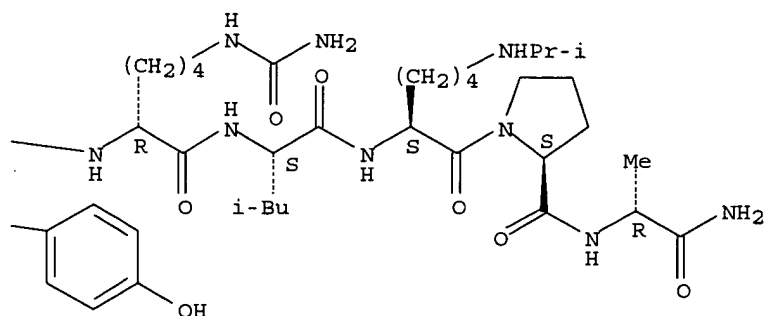
CA 2330131	AA	19991104	CA 1999-2330131	19990329 <--
AU 9937028	A1	19991116	AU 1999-37028	19990329 <--
AU 752415	B2	20020919		
BR 9909802	A	20001226	BR 1999-9802	19990329 <--
TR 200003063	T2	20010221	TR 2000-200003063	19990329 <--
EP 1082129	A1	20010314	EP 1999-919152	19990329 <--
EP 1082129	B1	20031029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002512975	T2	20020508	JP 2000-545555	19990329 <--
NZ 507405	A	20021025	NZ 1999-507405	19990329 <--
AT 252910	E	20031115	AT 1999-919152	19990329 <--
RU 2221588	C2	20040120	RU 2000-129658	19990329 <--
PT 1082129	T	20040331	PT 1999-919152	19990329 <--
ES 2207941	T3	20040601	ES 1999-919152	19990329 <--
NO 2000005145	A	20001013	NO 2000-5145	20001013 <--
PRAI US 1998-82743P	P	19980423	<--	
WO 1999-EP2133	W	19990329	<--	
AB	In the method of therapeutic management of infertility by intrauterine insemination the improvement consisting of (a) the dose-dependent suppression of endogenous gonadotropins, especially LH, with a LH-RH Antagonist allowing the maintenance of physiol. estrogen levels, (b) exogenous stimulation of the ovarian follicle growth, (c) ovulation induction with HCG, native LHRH, LHRH-Agonists or recombinant LH, (d) intrauterine insemination by sperm injection. The LHRH Antagonists may be preferably Cetorelix or Antarelix. The stimulation is performed by administration of HMG or recombinant FSH with or without recombinant LH or with antiestrogens as for example Chlomiphene as well as with the combination of antiestrogens as for example Chlomiphene with gonadotropins.			
IT	151272-78-5, Antarelix RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)			
RN	151272-78-5 HCAPLUS			
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)			

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:635574 HCAPLUS

DN 131:257877

TI Method for single-stage salt formation and purification of oligopeptides

IN Guenther, Kurt; Kunz, Franz-Rudolf; Drauz, Karlheinz; Mueller, Thomas

PA Degussa-Huels A.-G., Germany

SO Ger. Offen., 14 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19813849	A1	19990930	DE 1998-19813849	19980327 <--
	EP 955308	A1	19991110	EP 1999-105639	19990319 <--
	EP 955308	B1	20030502		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 239033	E	20030515	AT 1999-105639	19990319 <--
	ES 2199498	T3	20040216	ES 1999-105639	19990319 <--
	CA 2267084	AA	19990927	CA 1999-2267084	19990326 <--
	JP 11310595	A2	19991109	JP 1999-84386	19990326 <--
	US 6258933	B1	20010710	US 1999-276709	19990326 <--
PRAI	DE 1998-19813849	A	19980327	<--	

AB Medically important synthetic peptides are converted to their acetate salts and purified in a single step by liquid chromatog. using an acetate-containing mobile phase. Thus, synthetic cetorelix-HCl was chromatographed on Nucleosil 300-7-C18 or Purospher RP 18 with a mobile phase having a MeCN concentration gradient (30-700 mL MeCN + 970-300 mL H2O) and containing 50 mL AcOH. The main peak comprised 99.75% pure cetorelix with acetate and Cl⁻ contents of 6.5% and 220 ppm, resp.

IT 244792-32-3P

RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PREP (Preparation); PROC (Process)

(method for single-stage salt formation and purification of oligopeptides)

RN 244792-32-3 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, diacetate (salt) (9CI) (CA INDEX NAME)

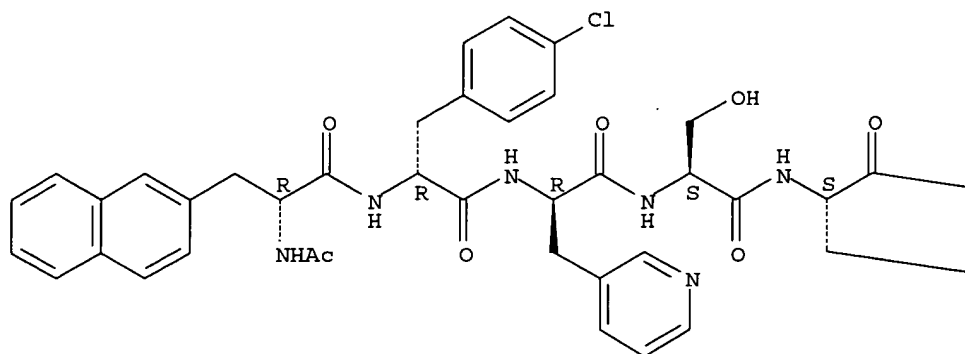
CM 1

CRN 151272-78-5

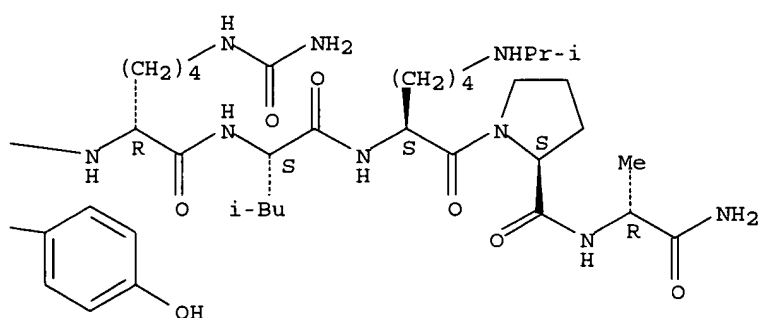
CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A

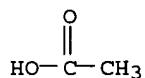


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2

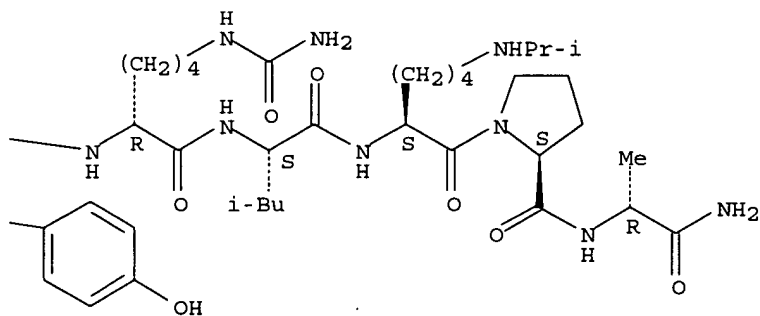


IT 244792-28-7P 244792-29-8P
 RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP
 (Preparation)
 (method for single-stage salt formation and purification of oligopeptides)
 RN 244792-28-7 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

The chemical structure shows a peptide backbone with several side chains. From left to right, the side chains are: a naphthyl group (two fused benzene rings), an N-acetyl group (NHAc), a 4-chlorophenyl group (a benzene ring with a chlorine atom at the para position), a pyridyl group (a six-membered aromatic ring with one nitrogen atom), and a hydroxyl group (OH). The peptide backbone consists of amide bonds connecting the amino groups of one residue to the carbonyl groups of the next. Stereochemistry is indicated with wedges and dashes at the chiral centers.

PAGE 1-B



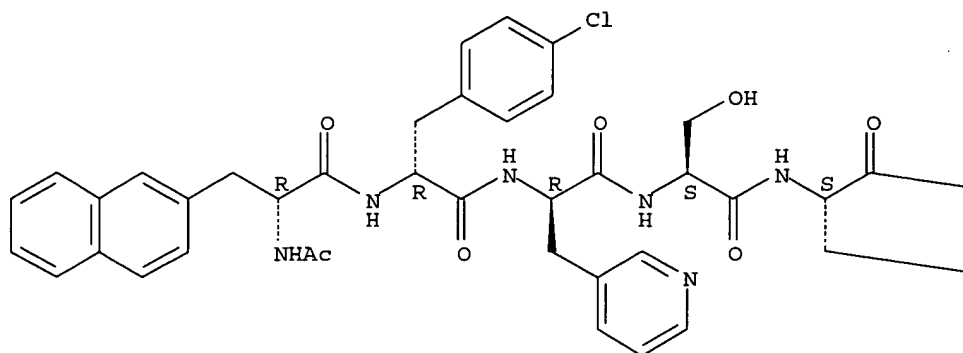
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CRN 151272-78-5

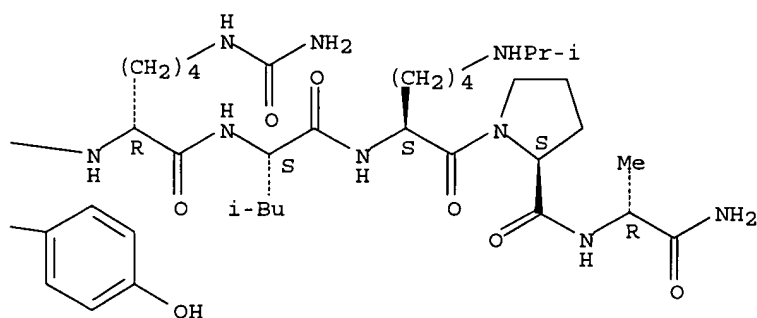
CMF C74 H100 C1 N15 O14

Absolute stereochemistry.

PAGE 1-A



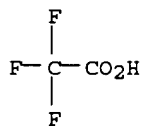
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L14 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1999:632654 HCAPLUS
 DN 131:332331
 TI Reduction of the developmental competence of sheep oocytes by inhibition
 of LH pulses during the follicular phase with a GnRH antagonist
 AU Oussaid, B.; Mariana, J. C.; Poulin, N.; Fontaine, J.; Lonergan, P.;
 Beckers, J. F.; Cognie, Y.
 CS INRA-Unite Physiologie Reproduction des Mammiferes Domestiques, Nouzilly,
 37380, Fr.
 SO Journal of Reproduction and Fertility (1999), 117(1), 71-77
 CODEN: JRPFA4; ISSN: 0022-4251
 PB Journals of Reproduction and Fertility Ltd.

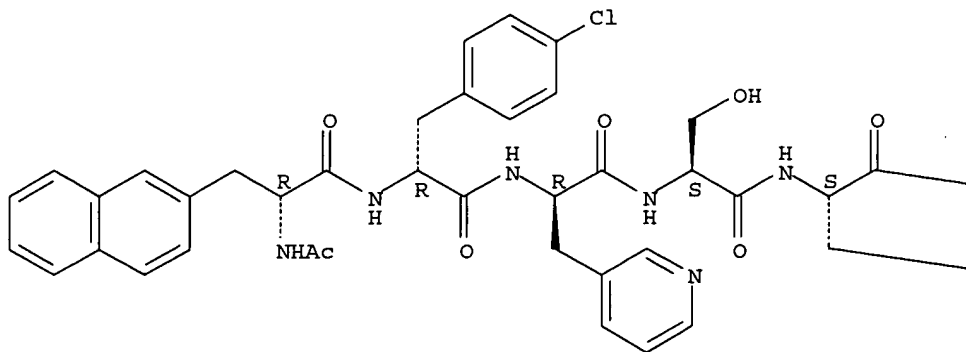
DT Journal
 LA English
 AB A GnRH antagonist (Antarelix) treatment was used during the breeding season of Romanov ewes, to investigate whether LH pulses are required the day before the preovulatory surge for normal early embryo development in vivo (Expt 1) and in vitro (Expt 2). In Expt 1, at the onset of oestrus after removal of a fluorogestone acetate sponge, group A0.5 (n = 22) received a s.c. injection of 0.5 mg Antarelix, and ovulation was induced with an i.v. injection of 3 mg pig LH 24 h later. The control group (group C, n = 20) were untreated. All ewes were mated naturally at 36 and 48 h after oestrus and embryos were recovered 8 days after sponge removal. There were significant differences in the decrease in LH and in the increase in FSH concentration after Antarelix treatment between treated and control groups. The ovulation rate and embryo recovery rate were not significantly different between the two groups but the blastocyst rate was lower ($P < 0.0001$) in group A0.5 than in group C, with more unfertilized or degenerated oocytes in group A0.5 (69.2%). In Expt 2, 24 h after sponge removal, group A (n = 10) and group B (n = 10) received one s.c. injection of 0.5 mg Antarelix. The control group (group C, n = 10) was left untreated. LH pulsatility was re-established in group B with hourly i.v. injections of 5 µg ovine LH for 24 h. Oocytes were collected by flushing the oviducts 28 h after the LH surge, and were fertilized and cultured in vitro for 7 days. Ovulation and cleavage rates were not significantly different among the three groups but a higher rate of blastocysts ($P < 0.01$) was obtained after Antarelix treatment when LH pulsatility was re-established (group B). Estradiol concentration was strongly depressed ($P < 0.0003$) after Antarelix treatment in group A, but was maintained after injection of LH pulses in group B, although at a lower value than before the preovulatory surge in the control group. In conclusion, inhibition of endogenous LH pulses 1 day before the preovulatory surge was not essential for ovulation and in vitro fertilization but was associated with a decrease in plasma estradiol concns. and inferior embryo development both in vivo and in vitro. When LH pulsatility was re-established, estradiol concns. increased and embryo development was restored.

IT 151272-78-5, Antarelix
 RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
 (reduction of developmental competence of sheep oocytes by inhibition of LH pulses during the follicular phase with a GnRH antagonist)

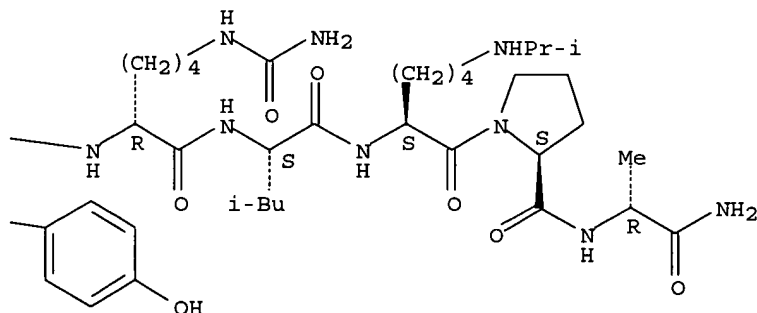
RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:614198 HCAPLUS
DN 131:307320
TI LH down-regulates gonadotropin-releasing hormone (GnRH) receptor, but not GnRH, mRNA levels in the rat testis
AU Botte, M-C.; Lerrant, Y.; Lozach, A.; Berault, A.; Counis, R.; Kottler, M-L.
CS Endocrinologie Cellulaire et Moleculaire de la Reproduction, Universite P and M Curie, CNRS ESA 7080, Paris, 75005, Fr.
SO Journal of Endocrinology (1999), 162(3), 409-415
CODEN: JOENAK; ISSN: 0022-0795
PB Society for Endocrinology
DT Journal
LA English
AB The demonstration of an inhibitory effect of gonadotropin-releasing hormone (GnRH) agonists upon steroidogenesis in hypophysectomized rats and the presence of mRNA coding for GnRH and GnRH receptors (GnRH-R) in rat gonads suggests that GnRH can act locally in the gonads. To assess this hypothesis, we investigated the effects of GnRH analogs, gonadotropins and testosterone on the levels of both GnRH and GnRH-R mRNA in the rat testis. Using dot blot hybridization, we measured the mRNA levels 2 to 120 h after the administration of the GnRH agonist, triptorelin. We observed an acute reduction of both GnRH and GnRH-R mRNAs 24 h after the injection (about 38% of control). However, the kinetics for testis GnRH-R mRNA were different from those previously found for pituitary GnRH-R mRNA under the same conditions. Initially, the concns. of serum LH and FSH peaked, then declined, probably due to the desensitization of the gonadotrope cells. In contrast, the GnRH antagonist, antarelix, after 8 h induced a 2.5-fold increase in GnRH-R mRNA, but not in GnRH mRNA, while gonadotropins levels were reduced. Human recombinant FSH had no significant effect on either GnRH or GnRH-R mRNA levels. Inversely, GnRH-R mRNA levels markedly decreased by 21% of that of control 24 h after hCG injection. Finally, 24 h after testosterone injection, a significant increase in GnRH-R mRNA levels (2.3 fold vs. control) was found, but a reduction in the concentration of serum LH, probably by neg. feedback on the pituitary, was observed. In contrast, GnRH mRNA levels were not significantly altered following testosterone treatment. Since LH receptors, GnRH-R and testosterone synthesis are colocalized in Leydig cells, our data suggest that LH could inhibit the GnRH-R gene expression or decrease the GnRH-R mRNA stability in the testis. However, this does not exclude the possibility that GnRH analogs could also affect the GnRH-R mRNA levels via direct binding to testicular GnRH-R. In contrast, the regulation of GnRH mRNA levels

appeared to be independent of gonadotropins. Taken together, our results suggest a regulation of GnRH and GnRH-R mRNA specific for the testis.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

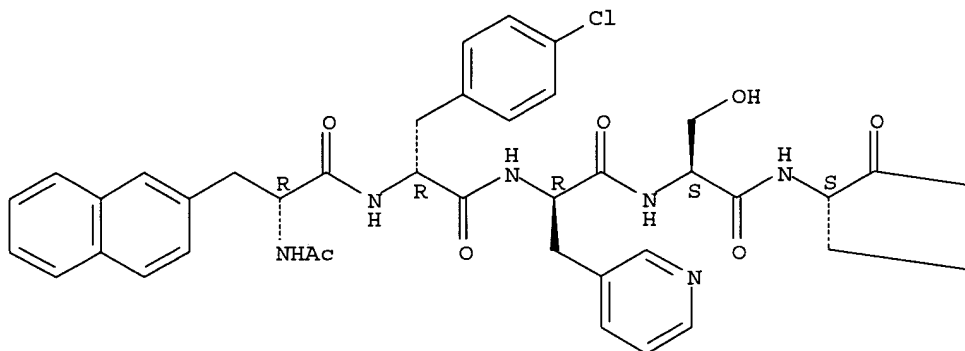
(effects of GnRH analogs, gonadotropins and testosterone on the levels of both GnRH and GnRH-R mRNA in the rat testis)

RN 151272-78-5 HCAPLUS

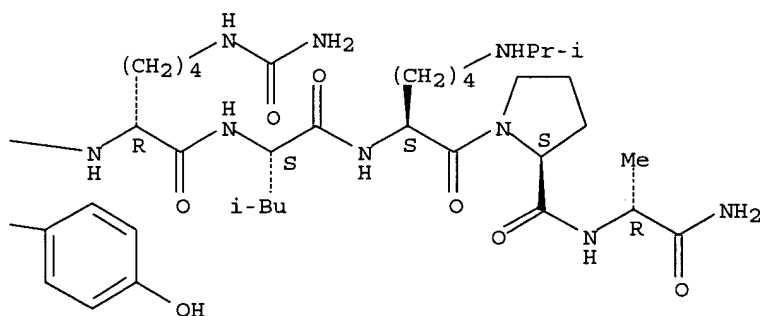
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:248859 HCAPLUS

DN 131:28106

TI Follicle-stimulating hormone-inhibin B interactions during the follicular phase of the primate menstrual cycle revealed by gonadotropin-releasing hormone antagonist and antiestrogen treatment

AU Fraser, H. M.; Groome, N. P.; McNeilly, A. S.

CS Medical Research Council Reproductive Biology Unit, Centre for Reproductive Biology, Edinburgh, EH3 9EW, UK

SO Journal of Clinical Endocrinology and Metabolism (1999), 84(4),

1365-1369

CODEN: JCEMAZ; ISSN: 0021-972X

PB Endocrine Society

DT Journal

LA English

AB The aim was to determine the pattern of inhibin A and inhibin B secretion during the ovulatory cycle of the macaque and to explore the effects of manipulating follicular phase FSH on inhibin B secretion by: (1) blocking the early follicular phase rise in FSH with GnRH antagonist treatment; (2) administering FSH in GnRH antagonist-treated animals; and (3) preventing the midfollicular phase decline in FSH by a specific antiestrogen. Treatment with GnRH antagonist, starting on day 25 of the cycle, abolished the early follicular phase rise in FSH and the associated increase in inhibin B. The same treatment, followed by exogenous FSH, restored the secretion of inhibin B. Treatment with antiestrogen, commencing during the midfollicular phase, induced a supraphysiol. rise in FSH, followed by a marked stimulation of inhibin B and estradiol secretion. Despite continued antiestrogen treatment, FSH secretion declined before peak values of inhibin B and estradiol were attained, implying a potential endocrine role for inhibin B, in addition to estradiol, in the neg. feedback regulation of FSH. These results show that follicular phase FSH is the major stimulus for inhibin B secretion.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

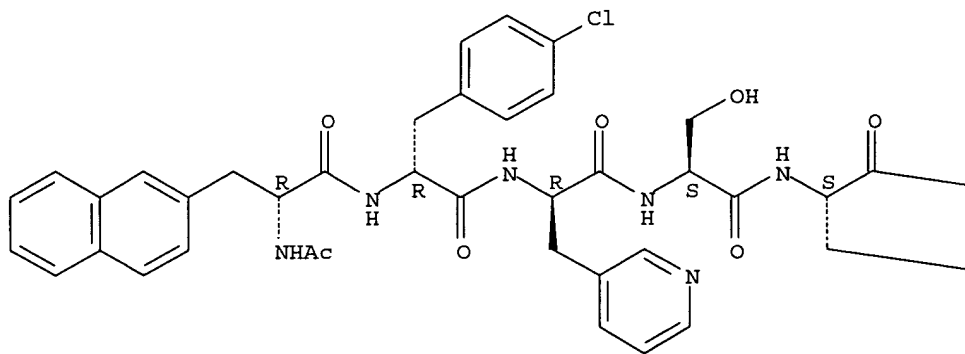
(FSH-inhibin B interactions during follicular phase of primate menstrual cycle revealed by LH-RH antagonist and antiestrogen treatment)

RN 151272-78-5 HCAPLUS

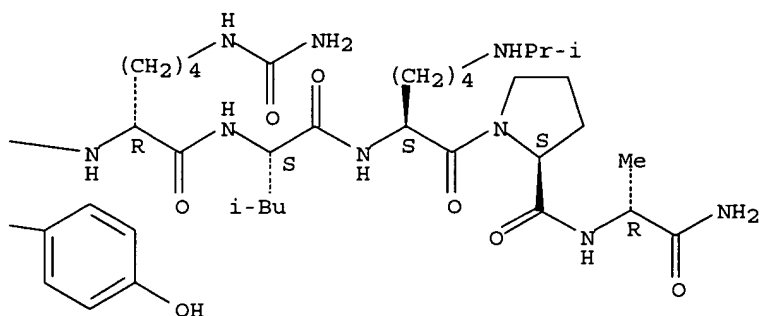
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:203164 HCAPLUS

DN 131:39885

TI Inhibin B levels in plasma of the male rat from birth to adulthood: effect of experimental manipulation of Sertoli cell number

AU Sharpe, R. M.; Turner, K. J.; McKinnell, C.; Groome, N. P.; Atanassova, N.; Millar, M. R.; Buchanan, D. L.; Cooke, P. S.

CS MRC Reproductive Biology Unit, Centre for Reproductive Biology, Edinburgh, EH3 9EW, UK

SO Journal of Andrology (1999), 20(1), 94-101

CODEN: JOAND3; ISSN: 0196-3635

PB American Society of Andrology

DT Journal

LA English

AB Sertoli cells undergo important changes in their number and function at different ages in the rat and may be the primary source of circulating inhibin B. The aims of this study were (1) to establish the profile of inhibin B levels from birth to adulthood in normal rats and (2) to identify whether exptl. manipulation of Sertoli cell nos. was able to alter this profile. Levels of inhibin B, measured by a specific two-site assay, increased fivefold in normal Wistar rats between day 3 and days 10-15, plateaued, and then declined in late puberty to reach adult levels which were approx. 60% of those observed on days 10-15. The increase in inhibin B levels in the neonatal period coincided with the period of Sertoli cell multiplication as indicated by incorporation of bromodeoxyuridine. Neonatal treatment of rats with a GnRH antagonist (GnRHa) reduced Sertoli cell number and adult testis weight by 48% and significantly reduced plasma levels of inhibin B at all ages through to adulthood. Induction of neonatal hypothyroidism in Sprague-Dawley rats by administration of propylthiouracil (PTU) up to day 25 of age increased final testis weight by 41% (indicative of increased Sertoli cell nos.) and resulted in elevation of plasma levels of inhibin B at all ages beyond 7 days of age. The degree of change in inhibin B levels in adult rats in the two exptl. treatment groups was approx. proportional to the change in final testis weight. Plasma FSH (FSH) showed changes opposite to inhibin B, with levels being lowered in PTU-treated rats and elevated (beyond day 25) in GnRHa-treated animals. The present results suggest that final Sertoli cell number per testis exerts an important effect on the circulating level of inhibin B (and FSH) in the rat. These findings are compared to the emerging data for the human male.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibin B levels in plasma of the male rat from birth to adulthood:

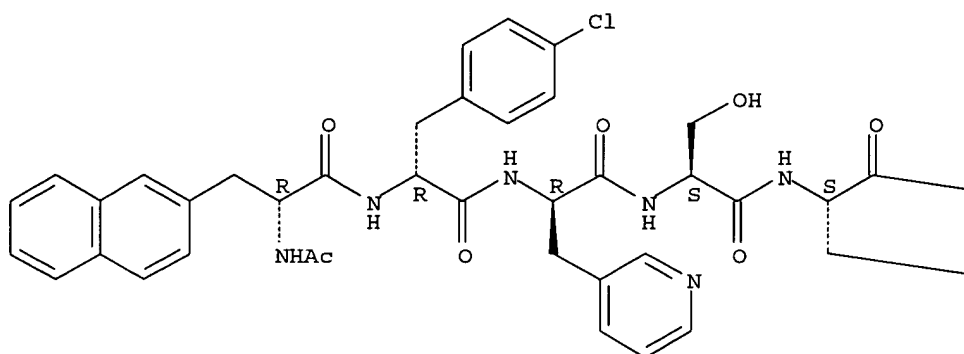
effect of exptl. manipulation of Sertoli cell number)

RN 151272-78-5 HCAPLUS

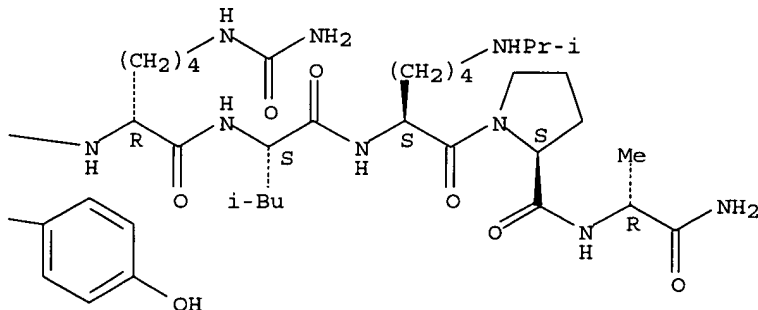
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:53463 HCAPLUS

DN 130:76610

TI Assays of gonadotropin-releasing hormone receptor and the use hormone effectors in the treatment of tumors of the nervous system

IN Van Groeninghen, Johannes Christianus

PA Van Groeninghen, Johannes Christianus, Germany

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9901764	A2	19990114	WO 1998-DE1902	19980703 <--
	WO 9901764	A3	19990514		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

DE 19728737 C1 19990211 DE 1997-19728737 19970704 <--
 CA 2295577 AA 19990114 CA 1998-2295577 19980703 <--
 AU 9892515 A1 19990125 AU 1998-92515 19980703 <--
 EP 993613 A2 20000419 EP 1998-944968 19980703 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI DE 1997-19728737 A 19970704 <--
 WO 1998-DE1902 W 19980703 <--

AB A method for recognizing and quantifying gonadotropin-releasing hormone receptors (GnRH receptors) on abnormal cells of a tumor originating in the brain, nervous system, meninges or in Kaposi's sarcoma is described. The method can be used in the diagnosis of these tumors. The use of GnRH agonists and antagonists or other ligands for GnRH receptors in the development of drugs for the treatment of these tumors is also described.

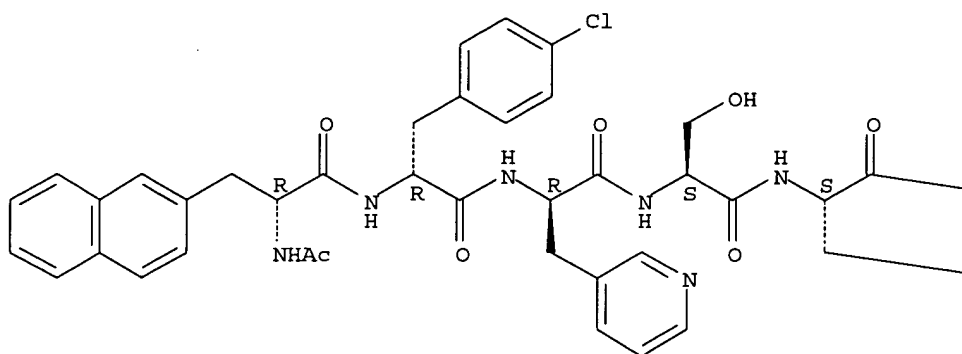
IT 151272-78-5, Antarelix
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (growth inhibition of glioblastoma cell lines by; assays of gonadotropin-releasing hormone receptor and use hormone effectors in treatment of tumors of nervous system)

RN 151272-78-5 HCAPLUS

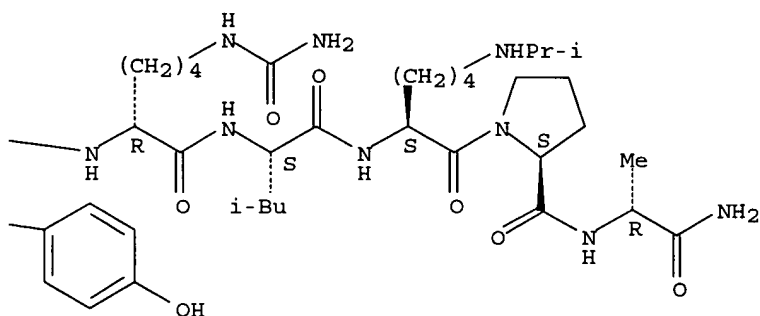
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:698996 HCAPLUS

DN 130:47627

TI Abnormalities in functional development of the Sertoli cells in rats treated neonatally with diethylstilbestrol: a possible role for estrogens in Sertoli cell development

AU Sharpe, R. M.; Atanassova, N.; McKinnell, C.; Parte, P.; Turner, K. J.; Fisher, J. S.; Kerr, J. B.; Groome, N. P.; Macpherson, S.; Millar, M. R.; Saunders, P. T. K.

CS MRC Reproductive Biology Unit, Centre for Reproductive Biology, Edinburgh, EH3 9EW, UK

SO Biology of Reproduction (1998), 59(5), 1084-1094

CODEN: BIREBV; ISSN: 0006-3363

PB Society for the Study of Reproduction

DT Journal

LA English

AB Diethylstilbestrol (DES) was administered neonatally (Days 2-12; 10 µg on alternate days) to rats, and developmental changes in Sertoli cell function were evaluated at 18, 25, and 35 days of age and compared to those observed in rats administered a GnRH antagonist (GnRHa; Days 2 and 5; 10 mg/kg) or a vehicle (controls). DES and GnRHa treatments resulted in similar redns. in both Sertoli cell nos. (40% for DES, 48% for GnRHa) and suppression of testicular growth at 18 and 25 days, though by 35 days the suppression was more pronounced in DES-treated animals. Plasma FSH levels were suppressed markedly at 18 and 25 days, but not at 35 days, in GnRHa-treated rats, whereas in DES-treated rats the FSH levels were suppressed significantly only at 35 days. Both treatments suppressed plasma levels of inhibin B, though this was more pronounced in DES- than in GnRHa-treated rats. In controls, Sertoli cell immunoexpression of inhibin α, sulfated glycoprotein-1 (SGP-1), and androgen receptor (AR) increased in intensity and changed to an adult, stage-dependent pattern by 25 days. In GnRHa-treated rats these changes were reduced in intensity but were similar to those in controls at 35 days. In DES-treated rats, the increase in intensity and stage-dependent pattern of immunoexpression of inhibin α, SGP-1, and AR were virtually absent at 25 days but were present by 35 days. Germ cell volume per Sertoli cell was reduced in GnRHa- and DES-treated rats compared with controls at 18 and 25 days but was significantly greater in DES- than in GnRHa-treated rats at 35 days. The proportion of apoptotic to viable germ cells was increased in GnRHa- and DES-treated rats compared with controls at 18 and 25 days; but at 35 days, values in GnRHa-treated rats had declined to control values whereas those for DES-treated rats remained 10-fold elevated. In adulthood, testis weight and daily sperm production were reduced by 43% and 44%, resp., in GnRHa-treated rats, but spermatogenesis was grossly normal. Comparable changes were observed in .apprx.25% of DES-treated rats, but the majority exhibited >60% reduction in testis weight with many Sertoli

cell-only tubules and very low daily sperm production Taken together, these data are interpreted as providing evidence for direct modulation of Sertoli cell (maturation) development by DES.

IT 151272-78-5, Antarelix

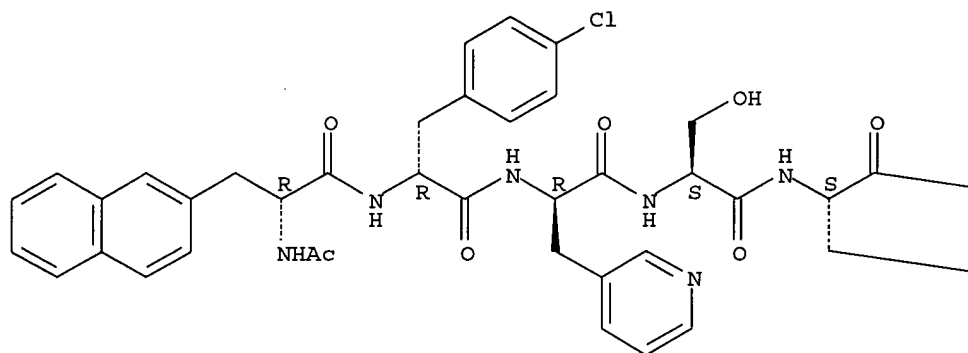
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(diethylstilbestrol and LH-RH antagonist neonatal induction of abnormalities in functional development of Sertoli cells in rats)

RN 151272-78-5 HCAPLUS

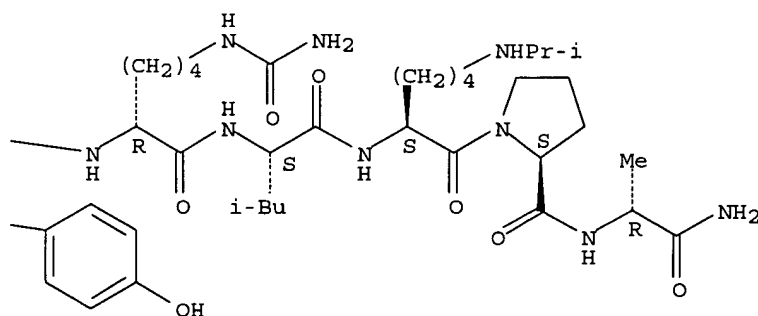
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:672495 HCAPLUS

DN 129:293891

TI Immobilized activity-stabilized LHRH antagonist complexes and their production

IN Engel, Juergen; Deger, Wolfgang; Reissmann, Thomas; Losse, Guenter; Naumann, Wolfgang; Murgas, Sandra

PA Asta Medica Aktiengesellschaft, Germany

SO PCT Int. Appl., 22 pp.

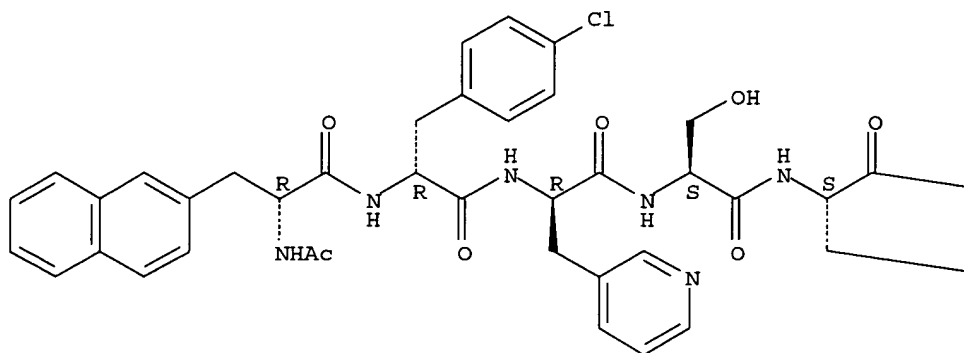
CODEN: PIXXD2

DT Patent
LA German
FAN.CNT 1

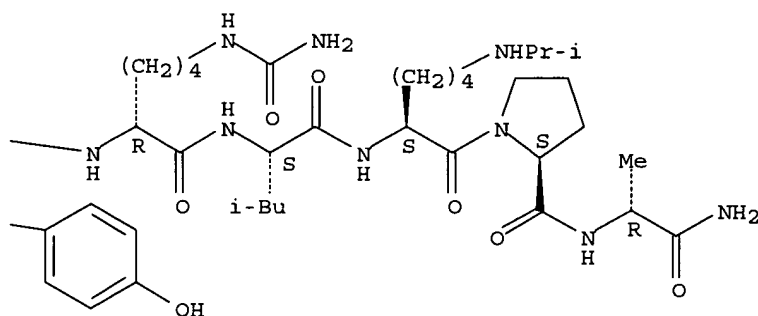
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842381	A1	19981001	WO 1998-EP1398	19980311 <--
	W: AU, BR, CA, CN, CZ, HU, IL, JP, MX, NO, NZ, PL, RU, SK, TR, UA				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19712718	A1	19981001	DE 1997-19712718	19970326 <--
	DE 19712718	C2	19990923		
	CA 2285054	AA	19981001	CA 1998-2285054	19980311 <--
	AU 9869207	A1	19981020	AU 1998-69207	19980311 <--
	AU 747808	B2	20020523		
	BR 9807887	A	20000222	BR 1998-7887	19980311 <--
	EP 981377	A1	20000301	EP 1998-914877	19980311 <--
	EP 981377	B1	20030910		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 337343	A	20011026	NZ 1998-337343	19980311 <--
	JP 2001520662	T2	20011030	JP 1998-544811	19980311 <--
	NZ 513901	A	20030228	NZ 1998-513901	19980311 <--
	RU 2207151	C2	20030627	RU 1999-123056	19980311 <--
	AT 249245	E	20030915	AT 1998-914877	19980311 <--
	PT 981377	T	20040227	PT 1998-914877	19980311 <--
	ES 2206912	T3	20040516	ES 1998-914877	19980311 <--
	SK 284461	B6	20050401	SK 1999-1316	19980311 <--
	ZA 9802225	A	19980403	ZA 1998-2225	19980317 <--
	TW 520288	B	20030211	TW 1998-87104303	19980323 <--
	US 6022860	A	20000208	US 1998-48244	19980326 <--
	NO 9904665	A	19990924	NO 1999-4665	19990924 <--
	US 6054555	A	20000425	US 1999-422990	19991022 <--
	HK 1025255	A1	20040924	HK 2000-104545	20000724 <--
PRAI	DE 1997-19712718	A	19970326	<--	
	WO 1998-EP1398	W	19980311	<--	
	US 1998-48244	A3	19980326	<--	
AB	LHRH antagonists, especially cetrorelix, are complexed with suitable biophilic carriers to enable sustained, targeted release of the active substance over a period of several weeks. The acidic polyamino acids, polyaspartic and polyglutamic acids, are selected for complexation with cetrorelix. The cetrorelix/polyamino acid complexes are produced from aqueous solns. by combining the solns. and precipitating the complexes which are subsequently centrifuged off and vacuum dried over P2O5, preferably by lyophilization. These acidic polyamino acids display good sustained-release properties in a static liberation system depending on the hydrophobicity and molar mass of the polyamino acids. Animal testing demonstrated the efficacy of the cetrorelix/polyamino acid complexes as a depot system. By complexation of cetrorelix with polyamino acids, testosterone suppression can be achieved in male rats over a period of 600 h. Active substance release can thus be controlled according to polymer type and molar mass.				
IT	151272-78-5D, Antarelix, complexes with poly(amino acids) RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (immobilized activity-stabilized LHRH antagonist complexes and their production)				
RN	151272-78-5 HCAPLUS				
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:644125 HCAPLUS

DN 130:33234

TI Induced luteolysis in the primate: rapid loss of luteinizing hormone receptors

AU Duncan, W. C.; Illingworth, P. J.; Young, F. M.; Fraser, H. M.

CS MRC Reproductive Biology Unit, Centre for Reproductive Biology, Edinburgh, EH3 9EW, UK

SO Human Reproduction (1998), 13(9), 2532-2540

CODEN: HUREEE; ISSN: 0268-1161

PB Oxford University Press

DT Journal

LA English

AB The mol. mechanisms involved in luteolysis are still unclear in the primate. This study aimed to investigate the effect of induced luteolysis on the ovarian LH receptor and the steroidogenic enzyme, 3 β -hydroxysteroid dehydrogenase (3 β -HSD) in the marmoset monkey. Luteolysis was induced in the mid-luteal phase either directly by systemic prostaglandin F2 α (PGF2 α), or indirectly by LH withdrawal using systemic gonadotrophin releasing hormone antagonist (GnRHant) treatment. The LH receptor was studied by isotopic mRNA in-situ hybridization and in-situ ligand binding and 3 β -HSD expression was studied using isotopic mRNA in-situ hybridization and immunohistochem. Induced luteolysis was associated with a reduction in the expression of LH

receptor ($P < 0.0001$) and 3β -HSD mRNA, closely followed by a reduction in the LH receptor ($P < 0.05$) and 3β -HSD protein concns. within 24 h. There were no differences in the findings whether luteolysis was induced with PGF 2α or GnRHant. This study shows that disparate mechanisms to induce luteolysis in the primate result in an identical rapid loss of the LH receptor and 3β -HSD. In conclusion, induced luteolysis leads to rapid loss of the steroidogenic pathway in luteal cells.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

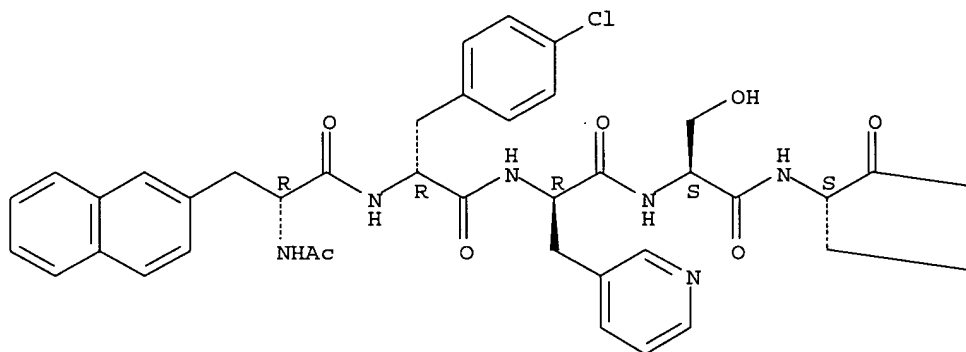
(GnRH antagonist; effect of luteolysis induced by PGF 2α or GnRH antagonist on the ovarian LH receptor and 3β -hydroxysteroid dehydrogenase in the marmoset monkey)

RN 151272-78-5 HCAPLUS

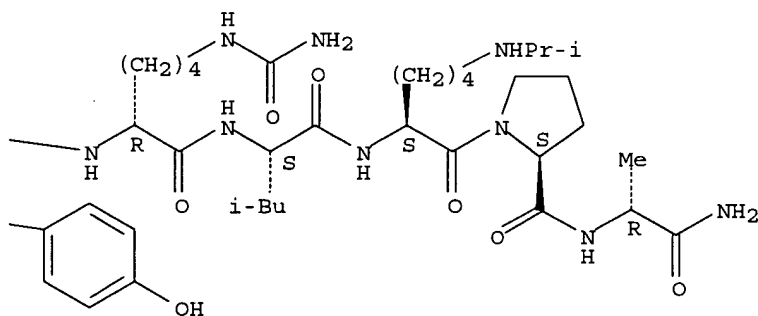
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:435777 HCAPLUS

DN 129:100038

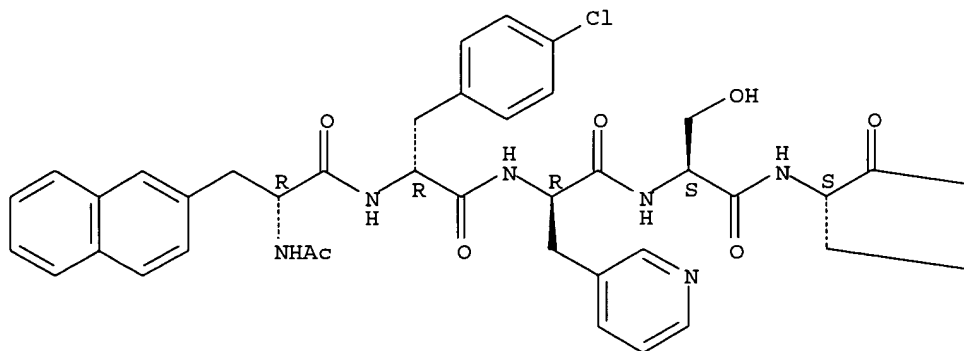
TI Long-acting injection suspensions of poorly soluble LHRH analogs

IN Engel, Jurgen; Klokke-Bethke, Karin; Reissman, Thomas; Hilgard, Peter
 PA Asta Medica A.-G., Germany
 SO U.S., 9 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 2

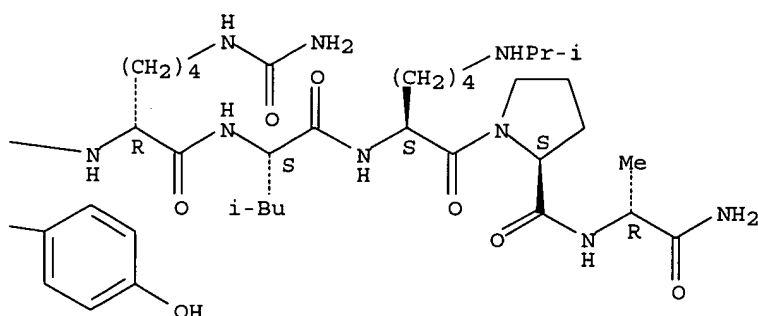
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PI	US 5773032	A	19980630	US 1996-661017	19960610 <--
	DE 4342092	A1	19950614	DE 1993-4342092	19931209 <--
	CZ 291025	B6	20021211	CZ 1996-1420	19941125 <--
	PL 186929	B1	20040430	PL 1994-314913	19941125 <--
	IL 111928	A1	19991130	IL 1994-111928	19941208 <--
	FI 9602354	A	19960606	FI 1996-2354	19960606 <--
	FI 116121	B1	20050930		
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	WO 1994-EP3904	W	19941125	<--	
	US 1996-661017	A	19960610	<--	
AB	Poorly soluble salts of LHRH analogs, for example cetorelix embonate, display an intrinsic sustained release effect in the grain size 5 µm to 200 µm. Cetorelix and embonic acid were dissolved in a molar ratio of 1:1.6 in a mixture of di-Me acetamide and optionally water and the solution dropped into water. The yellow precipitate was filtered off and dried and the precipitate thus obtained was pasted with 70% ethanol, dried at 35° and sieved through a sieve of mesh size 80 to 125 µm. Suspensions of the ppts. were applied s.c. to male rats in the dose of 0.5 mg cetorelix/kg body weight to decrease the testosterone level. The effect of testosterone suppression was achieved 6 h after the application, and suppression under 1 ng/mL could still be determined in two animals for 24 h, and in three further animals up to 48 h or two days.				
IT	151272-78-5, Antarelix RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (long-acting injection suspensions of poorly soluble LHRH analogs)				
RN	151272-78-5 HCAPLUS				
CN	D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



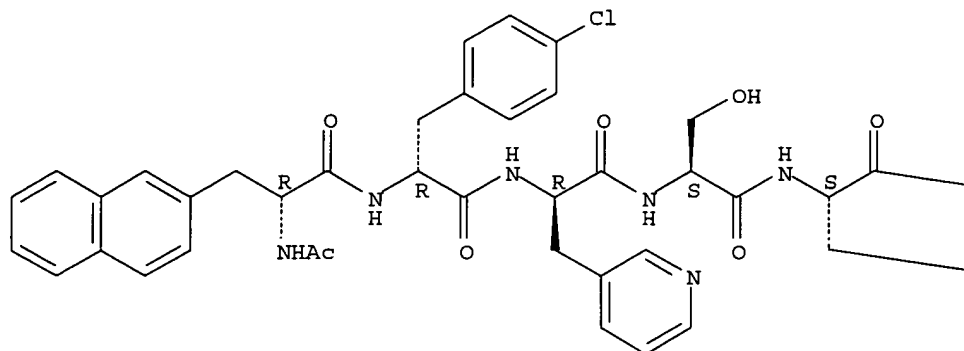
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:706035 HCAPLUS
DN 128:10573
TI Cell death during luteal regression in the marmoset monkey (*Callithrix jacchus*)
AU Young, F. M.; Illingworth, P. J.; Lunn, S. F.; Harrison, D. J.; Fraser, H. M.
CS MRC Reproductive Biology Unit, Centre for Reproductive Biology, Edinburgh, EH3 9EW, UK
SO Journal of Reproduction and Fertility (1997), 111(1), 109-119
CODEN: JRPFA4; ISSN: 0022-4251
PB Journals of Reproduction and Fertility
DT Journal
LA English
AB The mechanism controlling luteal regression in primates is unknown but may involve cell death by apoptosis. Marmoset ovaries containing corpora lutea were studied at different stages of the normal ovarian cycle. Two addnl. groups of animals underwent induced luteolysis with either the prostaglandin F2 α analog, cloprostenol, or the GnRH antagonist, antarelix, at the mid-luteal phase. Apoptosis in ovarian sections was estimated both by counting the number of cells exhibiting morphol. features of apoptosis and by in situ labeling the 3' ends of the DNA fragments with digoxigenin-11-dUTP. Apoptosis was found to be significantly increased in corpora lutea in the early follicular phase (equivalent to the later stage of luteal lifespan) compared with the mid-luteal phase corpora lutea, as judged by either computerized morphometry or 3' end labeling. Apoptosis was also increased by the administration of either cloprostenol or antarelix when using the 3' end labeling end point, but only after cloprostenol when using computerized morphometry. A further form of cell death, characterized by the formation of cytoplasmic vacuoles, was also observed in corpora lutea undergoing both induced and spontaneous regression. These results demonstrate that apoptosis within the primate corpus luteum is increased in both physiol. and induced luteal regression. In addition, they show that an alternative form of cell death is involved in both spontaneous and induced luteal regression, although the relative importance of the two mechanisms remains to be determined
IT 151272-78-5, Antarelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cell death during spontaneous and cloprostenol- or antarelix-induced luteal regression in marmoset monkeys)
RN 151272-78-5 HCAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-

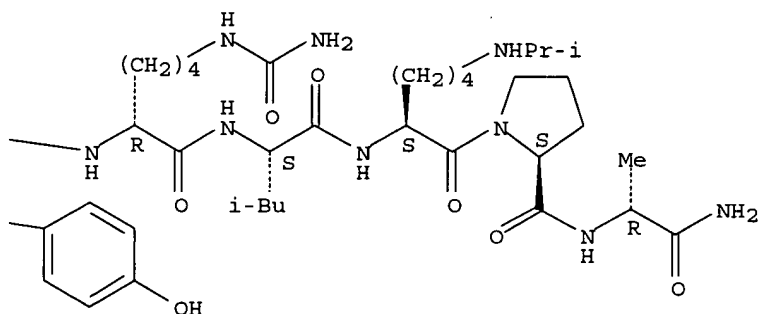
phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-
D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:573390 HCAPLUS
DN 127:257679
TI Characterization of gonadotropin-releasing hormone analogs based on a
sensitive cellular luciferase reporter gene assay
AU Beckers, Thomas; Reilander, Helmut; Hilgard, Peter
CS Department of Cancer Research, ASTA Medica AG, Frankfurt/Main, D-60314,
Germany
SO Analytical Biochemistry (1997), 251(1), 17-23
CODEN: ANBCA2; ISSN: 0003-2697
PB Academic
DT Journal
LA English
AB A novel cellular assay for the functional characterization of agonistic
and antagonistic analogs of gonadotropin-releasing hormone (GnRH) was
developed. This assay is based on a fusion of the c-fos immediate-early
gene promoter to Photinus pyralis luciferase (Luc) as a reporter gene,
stably transfected in a recombinant cell line expressing the human GnRH
receptor. Transcription of endogenous c-fos and fos-Luc fusion gene are

transiently induced quite similar by fetal calf serum or the superagonistic analog [D-Trp6] GnRH in a selected cell line. The reporter gene was therefore used to monitor agonist-induced signaling via the human GnRH receptor. Whereas Luc activity was induced in a dose-dependent manner by GnRH or [D-Trp6] GnRH, different antagonistic peptides completely inhibited this stimulation. The antagonistic potency (IC50) of various peptides with Cetrorelix and Antarelix as lead compds. in general correlated well with the binding affinity (KD) as determined from ligand binding expts. The specificity of an inhibitory effect was confirmed by GnRH receptor-independent stimulation with the phorbol ester 12-O-tetradecanoylphorbol 13-acetate or basic fibroblast growth factor. Since this new reporter gene assay is sensitive and simple and can be performed in a microtiter plate, it will significantly facilitate screening and functional characterization of GnRH analogs.

IT 151272-78-5, Antarelix

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

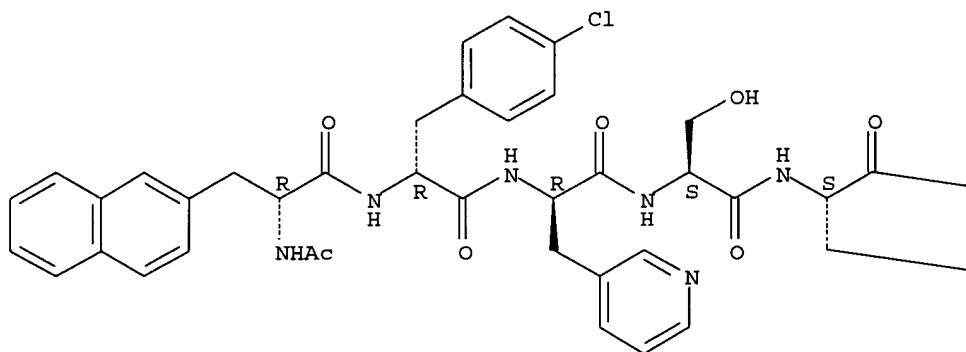
(LH-RH analog characterization based on sensitive cellular luciferase reporter gene assay)

RN 151272-78-5 HCAPLUS

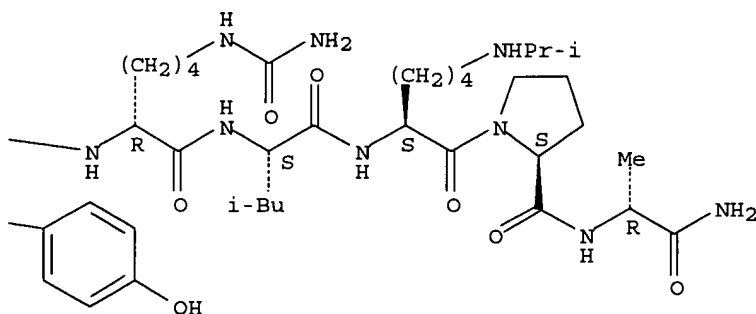
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

Noble Jarrell

21/11/2005

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:168540 HCAPLUS

DN 126:152828

TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals

IN Roeske, Roger W.

PA Indiana University Foundation, USA; Roeske, Roger W.

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640757	A2	19961219	WO 1996-US9852	19960607 <--
	WO 9640757	A3	19970220		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5843901	A	19981201	US 1995-480494	19950607 <--
	CA 2219460	AA	19961219	CA 1996-2219460	19960607 <--
	AU 9661680	A1	19961230	AU 1996-61680	19960607 <--
	AU 715399	B2	20000203		
	EP 794961	A2	19970917	EP 1996-919311	19960607 <--
	EP 794961	B1	20020828		
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 11507374	T2	19990629	JP 1996-502050	19960607 <--
	EP 1188768	A2	20020320	EP 2001-204149	19960607 <--
	EP 1188768	A3	20021023		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 222924	E	20020915	AT 1996-919311	19960607 <--
	ES 2177789	T3	20021216	ES 1996-919311	19960607 <--
	PT 794961	T	20030131	PT 1996-919311	19960607 <--
	US 6423686	B2	20020723	US 1998-973378	19980406 <--
	US 2002115615	A1	20020822		
	US 6455499	B1	20020924	US 1999-256599	19990223 <--
	US 2003040482	A1	20030227	US 2002-115553	20020402 <--
	US 2003181385	A1	20030925	US 2002-117364	20020405 <--
PRAI	US 1995-480494	A	19950607	<--	
	EP 1996-919311	A3	19960607	<--	
	WO 1996-US9852	W	19960607	<--	
	US 1998-973378	A3	19980406	<--	
OS	MARPAT 126:152828				
AB	Many novel LH-releasing hormone(LHRH) antagonist peptide analogs or peptide mimetics, pharmaceutical compns. thereof, and methods of use thereof, are disclosed. The LHRH antagonist comprises a peptide compound, wherein a residue of the peptide compound corresponding to the amino acid at position 6 of natural mammalian LHRH comprises a hydrophilic N-acyl moiety, a dipolar moiety, a sulfonium moiety, a receptor-modifying moiety or a small polar moiety. LHRH antagonist peptides are useful as inhibitors of sex hormone-dependent cancers (e.g., prostate cancer). LHRH antagonist peptides are also useful as contraceptive agents. The peptides can be used to treat other LHRH-related disorders as well, such as precocious puberty or premenstrual syndrome. The anti-ovulatory and histamine release activity of LHRH antagonists are compared. S.c. injections of LHRH antagonists suppressed plasma testosterone levels.				
IT	186836-91-9P				
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)				

RN 186836-91-9 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-
 3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-acetyl-D-lysyl-L-leucyl-N6-
 (1-methylethyl)-L-lysyl-L-prolyl-, mono(trifluoroacetate) (salt) (9CI)
 (CA INDEX NAME)

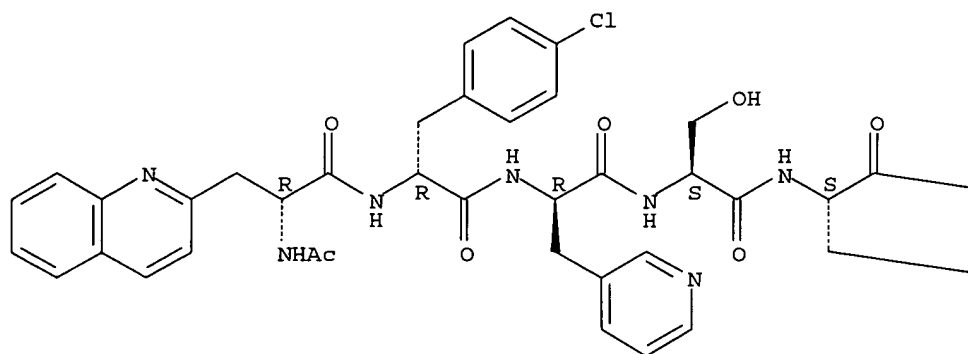
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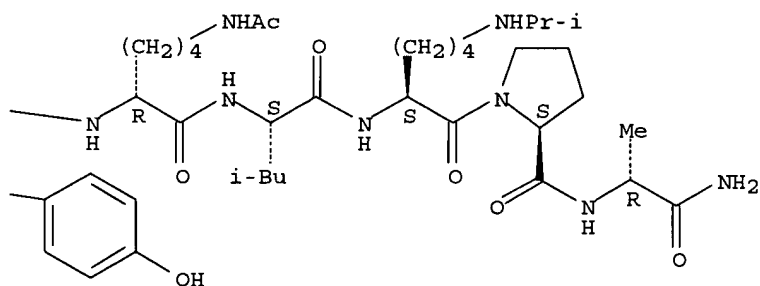
CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A



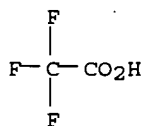
PAGE 1-B



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CRN 76-05-1

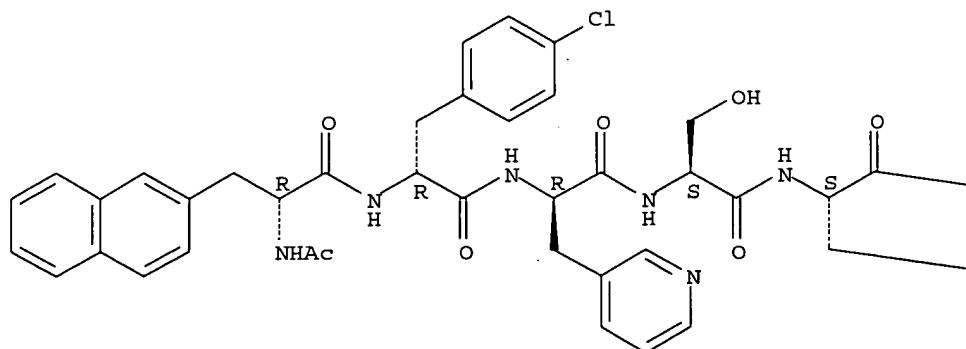
CMF C2 H F3 O2



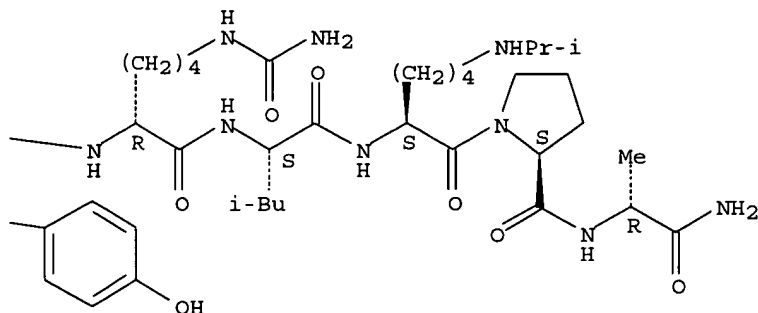
L14 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1996:744116 HCAPLUS
 DN 126:87547
 TI Expression of tissue inhibitor of metalloproteinases-1 in the primate ovary during induced luteal regression
 AU Duncan, W. C.; Illingworth, P. J.; Fraser, H. M.
 CS MRC Reprod. Biol. Unit., Cent. Reprod. Biol., Edinburgh, EH3 9EW, UK
 SO Journal of Endocrinology (1996), 151(2), 203-213
 CODEN: JOENAK; ISSN: 0022-0795
 PB Journal of Endocrinology
 DT Journal
 LA English
 AB This study sought to determine (1) the effect of induced luteal regression on ovarian tissue inhibitor of metalloproteinases-1 (TIMP-1) expression in the primate and (2) the expression of TIMP-1 in other steroidogenic and non-steroidogenic tissues. Marmoset ovaries were studied on day 10 of the normal luteal phase and 12 and 24 h after induced luteolysis, with either gonadotropin-releasing hormone (GnRH) antagonist or prostaglandin F2 α analog. Ovaries from different stages of the normal ovarian cycle were also studied. Expression of TIMP-1 was investigated by isotopic in situ hybridization. TIMP-1 expression was also examined in a wide range of other marmoset tissues by Northern blotting and in situ hybridization. TIMP-1 was found to be highly expressed in the marmoset corpus luteum. Luteolysis induced with either PGF2 α or GnRH antagonist was associated with a significant fall in TIMP-1 expression in luteal tissue. TIMP-1 mRNA was also localized to ovarian follicles throughout the ovarian cycle. Expression occurred in the thecal layer of smaller follicles (<1.5 mm) and the granulosa layer of larger pre-ovulatory follicles. In atretic follicles, TIMP-1 was highly expressed and the interface between the thecal and granulosa cells. TIMP-1 was found to be predominantly expressed in steroidogenic tissues, particularly the ovary, adrenal, and placenta. These data support a role for changes in TIMP-1 expression in tissue remodelling in the ovary and are consistent with an addnl. function of TIMP-1 as a facilitator of steroidogenesis.
 IT 151272-78-5, Antarelix
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (tissue inhibitor of metalloproteinases-1 expression in primate ovary during induced luteal regression)
 RN 151272-78-5 HCAPLUS
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:249914 HCAPLUS

DN 124:279399

TI A new method for controlling the precise time of occurrence of the preovulatory gonadotropin surge in superovulated goats

AU Baril, G.; Pougnaud, J. L.; Freitas, V. J. F.; Leboeuf, B.; Saumande, J.

CS Station de Physiologie de la Reproduction des Mammiferes Domestiques, Institut National de la Recherche Agronomique, Nouzilly, 37380, Fr.

SO Theriogenology (1996), 45(3), 697-706

CODEN: THGNBO; ISSN: 0093-691X

PB Elsevier

DT Journal

LA English

AB In goats treated to induce superovulation, insemination at a predetd. time after the end of progestagen treatment leads to a low fertilization rate. To solve this problem we developed a new treatment based on the control of the occurrence of the endogenous LH peak with a GnRH antagonist (Antarelix). The first experiment was designed to determine the dose of LH required to mimic a spontaneous LH preovulatory discharge; the injection of 3 mg, i.v. of pLH induced a peak of the same amplitude and duration as the spontaneous peak. Subsequently, in the second experiment, we compared 2 doses of Antarelix (0.5 and 1 mg, s.c.) administered 12 h after sponge removal (9 goats/treatment group). The dose of 0.5 mg was selected for further expts. because it was effective in the inhibition of the endogenous LH peak and had no detrimental effect on the quality of embryos. In the final experiment, 48 goats received the new treatment and were inseminated (intrauterine) only once 16 h after LH injection; 41 were flushed and produced 5.3 (m) transferable embryos. The developmental stage and the number of cells/embryo were within the range that has been reported for embryos produced with conventional treatments. In conclusion, with the described method, it is possible to inseminate goats at a predetd. time without decreasing the number of transferable embryos. This technique will encourage the development of embryo transfer within genetic programs, and it will be a valuable tool for the production of zygotes for gene transfer.

IT 151272-78-5, Antarelix

RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)

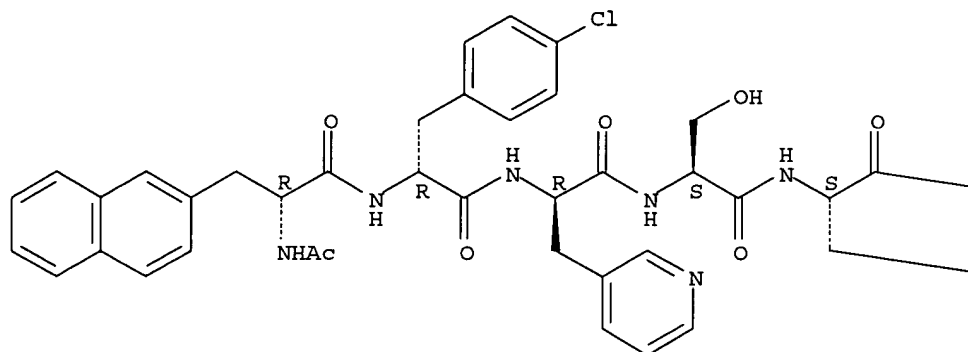
(preovulatory gonadotropin surge synchronization with LH-RH antagonist in superovulated goats)

RN 151272-78-5 HCAPLUS

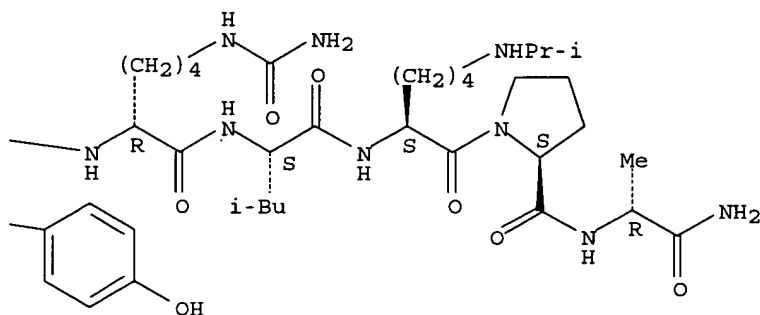
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L14 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:767118 HCAPLUS

DN 124:22062

TI Selection and characterization of mammalian cell lines with stable over-expression of human pituitary receptors for gonadoliberein

AU Beckers, Thomas; Marheineke, Kathrin; Reilaender, Helmut; Hilgard, Peter

CS ASTA Medica AG, Frankfurt/Main, Germany

SO European Journal of Biochemistry (1995), 231(3), 535-43

CODEN: EJBICAI; ISSN: 0014-2956

PB Springer

DT Journal

LA English

AB The cDNA encoding the receptor for gonadoliberein (GnRH or LH-RH) was isolated from a human pituitary cDNA library and heterologously expressed in the murine fibroblast cell line LTK-. By using a dicistronic expression strategy utilizing the internal ribosomal-entry-site sequence of poliovirus, single cell clones with stable and high expression of human gonadoliberein receptors were selected. The gonadoliberein antagonist Cetrorelix showed high-affinity binding to the heterologously expressed human gonadoliberein receptor with a K_d of 0.1 nM in radioligand saturation-binding expts. The pharmacol. profile using ¹²⁵I-Cetrorelix as radioligand and the authentic gonadoliberein or agonistic and antagonistic derivs. as competitors, showed a distinct rank order of binding potencies. Superagonistic gonadoliberein derivs. had more than 10 times higher binding

affinities in comparison to gonadoliberein with a K_d of 3.47 nM. The gonadoliberein receptor expressed in stably transfected LTK- cells coupled to the inositol phosphate signal-transduction pathway. Gonadoliberein stimulated the synthesis of inositol 1,4,5-trisphosphate in a dose-dependent way with an EC_{50} of 5 nM. This stimulatory effect of gonadoliberein was completely antagonized by Cetrorelix in equimolar concns., demonstrating the high potency of this competitive receptor antagonist. A transient expression of the c-fos protooncogene in growth-arrested cells was induced by gonadoliberein or [D-Trp6]gonadoliberein. The gonadoliberein receptor couples to a putative mitogenic signal-transduction pathway in this heterologous cell system.

IT 151272-78-5, Antarelix

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

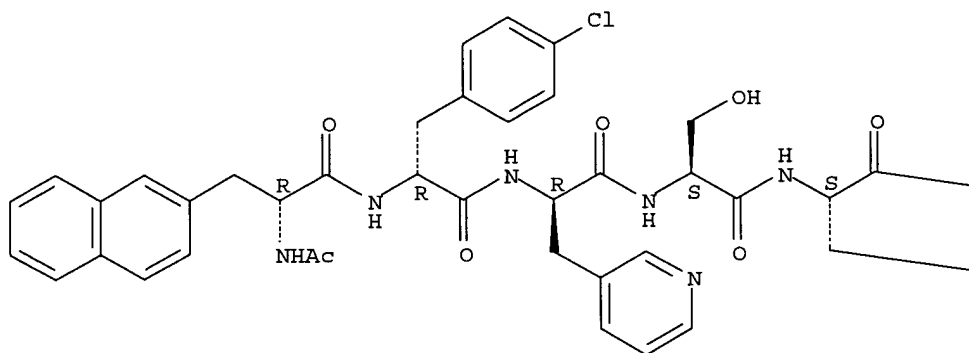
(gonadoliberein receptors function and characterization after stable over-expression in fibroblast cell line)

RN 151272-78-5 HCAPLUS

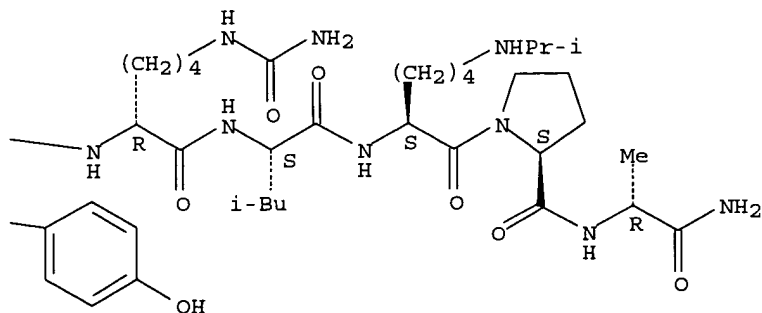
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=> b uspatall

FILE 'USPATFULL' ENTERED AT 11:41:46 ON 21 NOV 2005

Noble Jarrell

21/11/2005

CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 11:41:46 ON 21 NOV 2005

CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitrn fhitr 122 tot

L22 ANSWER 1 OF 8 USPATFULL on STN

AN 2004:285839 USPATFULL

TI Implants for non-radioactive brachytherapy of hormonal-insensitive cancers

IN Deghenghi, Romano, St. Cergue, SWITZERLAND

PI US 2004224000 A1 20041111

AI US 2003-430132 A1 20030505 (10)

DT Utility

FS APPLICATION

LREP WINSTON & STRAWN, PATENT DEPARTMENT, 1400 L STREET, N.W., WASHINGTON, DC, 20005-3502

CLMN Number of Claims: 62

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 515

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Implants are described for use in a novel therapy of hormone-insensitive tumors. The implants are inserted near, around or inside such tumors to provide a high local concentration and sustained release of a gonadotrophin-release hormone agonist or antagonist and a direct inhibitory action on the growth of such tumors. As the implants are not radioactive, the deleterious side-effects of radioactive treatments are avoided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, Teverelix

(GRH antagonist; implants for non-radioactive brachytherapy of hormonal-insensitive cancers)

IT 144743-92-0, Teverelix

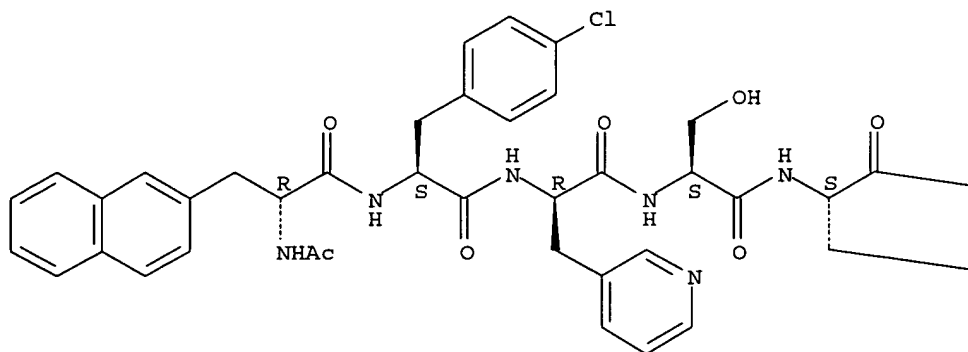
(GRH antagonist; implants for non-radioactive brachytherapy of hormonal-insensitive cancers)

RN 144743-92-0 USPATFULL

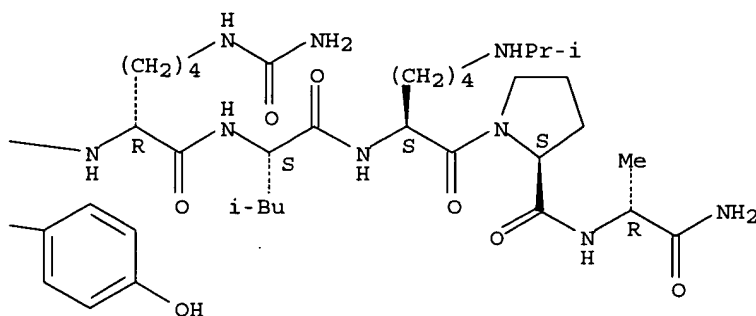
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L22 ANSWER 2 OF 8 USPATFULL on STN

AN 2003:64343 USPATFULL

TI Sustained release of microcrystalline peptide suspensions

IN Deghenghi, Romano, St. Cergue, SWITZERLAND

Boutignon, Francois, Ermont, FRANCE

PI US 2003044463 A1 20030306

AI US 2002-80130 A1 20020219 (10)

PRAI US 2001-317616P 20010906 (60)

DT Utility

FS APPLICATION

LREP WINSTON & STRAWN, PATENT DEPARTMENT, 1400 L STREET, N.W., WASHINGTON, DC, 20005-3502

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 379

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method of preventing gel formation of a hydrophobic peptides by contacting the hydrophobic peptide with a counter-ion in an amount and at a molar ratio with the peptide that are sufficient to provide a fluid, milky microcrystalline aqueous suspension of the peptide without formation of a gel. The invention also relates to a fluid, milky microcrystalline aqueous suspension of a hydrophobic peptide and a counter-ion in water, wherein the peptide and counter-ion are present in amounts and at a molar ratio sufficient to form, upon mixing, the suspension without formation of a gel.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 500717-24-8 500717-25-9

(sustained release of microcryst. peptide suspensions)

IT 144743-92-0, Teverelix

(sustained release of microcryst. peptide suspensions)

IT 500717-24-8

(sustained release of microcryst. peptide suspensions)

RN 500717-24-8 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, trifluoroacetate (9CI) (CA INDEX NAME)

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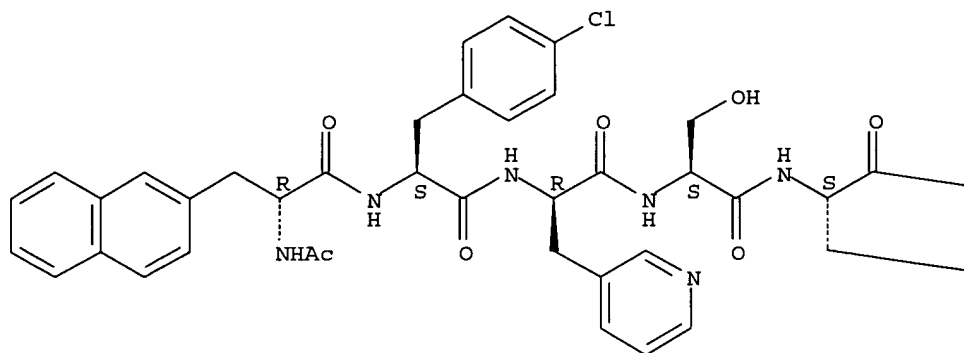
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CMF C74 H100 Cl N15 O14

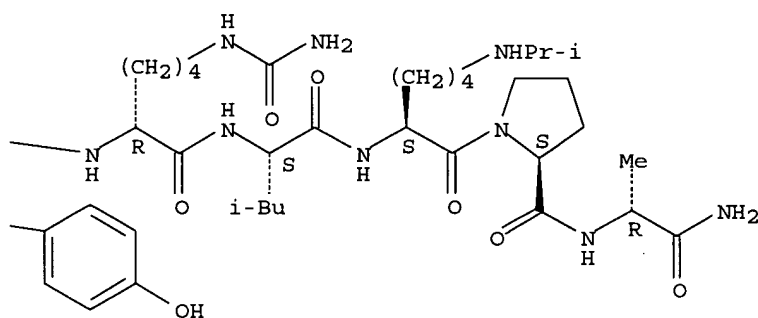
CDES 5:D,L,D,L,L,D,L,L,L,D

Absolute stereochemistry.

PAGE 1-A

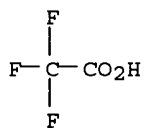


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L22 ANSWER 3 OF 8 USPATFULL on STN

AN 2001:170756 USPATFULL

TI Compressed microparticles for dry injection

IN Boutignon, Francois, Ermont, France

PI US 2001026804 A1 20011004

US 6627600 B2 20030930

AI US 2001-764111 A1 20010119 (9)

RLI Continuation-in-part of Ser. No. US 2000-491978, filed on 27 Jan 2000, ABANDONED

PRAI AU 2000-22 20000118

DT Utility

FS APPLICATION

Noble Jarrell

21/11/2005

LREP WINSTON & STRAWN, 200 PARK AVENUE, NEW YORK, NY, 10166-4193

CLMN Number of Claims: 40

ECL Exemplary Claim: 1

DRWN 9 Drawing Page(s)

LN.CNT 940

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a pharmaceutical implant for controllably releasing a drug in a subject and methods for manufacturing and administering the implant. The implant is made of associated microparticles of a drug dispersed in a biodegradable polymer. The microparticles are sufficiently associated so that the implant maintains a predetermined shape but are not fused together so as to form a single monolithic structure. The drug can be controllably released in a subject by administration of the pharmaceutical implant without the need of a suspending fluid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**
(compressed microparticles for dry injection)

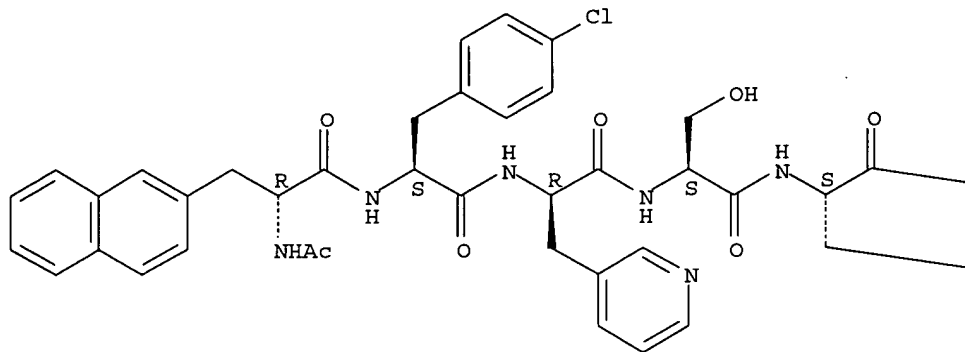
IT 144743-92-0, **Teverelix**
(compressed microparticles for dry injection)

RN 144743-92-0 USPATFULL

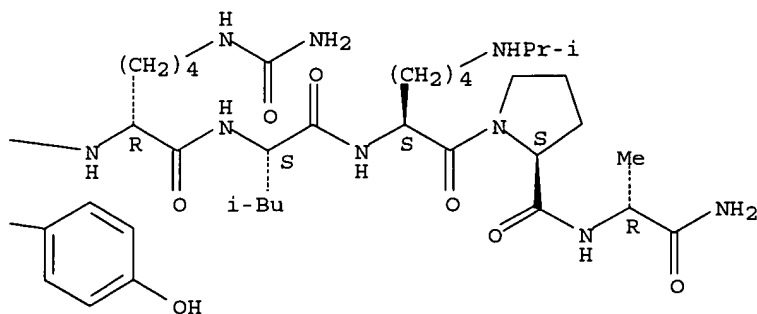
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L22 ANSWER 4 OF 8 USPATFULL on STN
AN 2000:167538 USPATFULL
TI Implants containing bioactive peptides
IN Deghenghi, Romano, Cheseaux Dessus B1, St. Cergue, Switzerland
PI US 6159490 20001212
AI US 2000-543707 20000405 (9)
RLI Continuation of Ser. No. US 1999-311744, filed on 14 May 1999, now patented, Pat. No. US 6077523 which is a division of Ser. No. US 1997-897942, filed on 21 Jul 1997, now patented, Pat. No. US 5945128
PRAI US 1996-25444P 19960904 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Azpuru, Carlos A.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

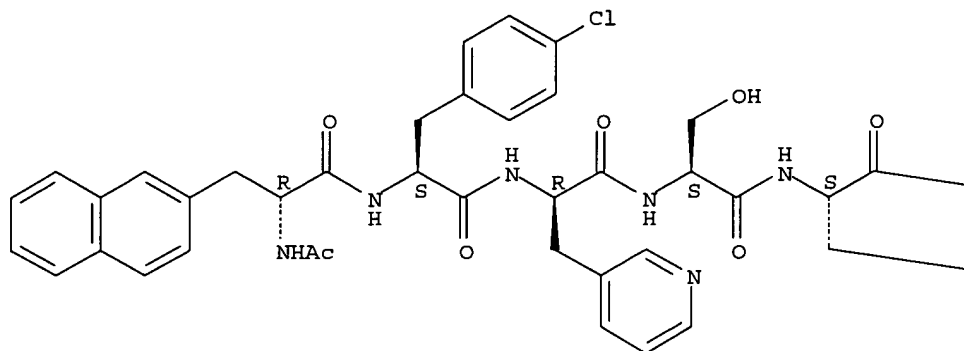
AB A pharmaceutical implant for the delivery of an effective amount of a bioactive peptide or peptide analog over a period of 1 to 12 months. This implant has a diameter of about 1 to 2 mm, a length of between about 10 and 25 mm and is obtainable from a process which includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 μ m; sterilizing the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing γ -radiation; wetting the ground and sterilized copolymer with a sterile aqueous slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixture of the copolymer and between about 10 and 50% of the bioactive peptide or peptide analog; drying the mixture at reduced pressure and at temperature not exceeding 25° C.; aseptically extruding the dried mixture at a temperature between about 70 and 110° C.; and aseptically cutting a cylindrical rod from the extruded mixture to form the pharmaceutical implant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

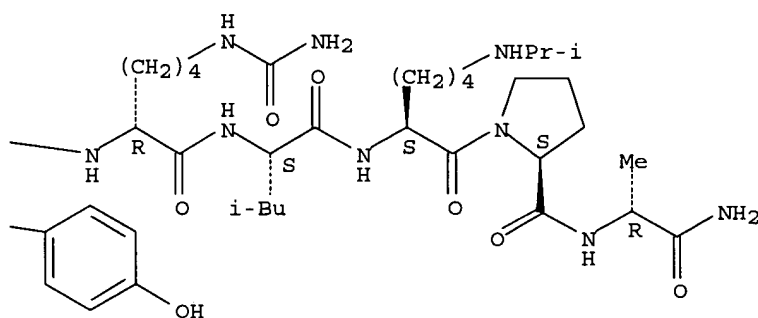
IT 144743-92-0D, Teverelix, salts
(pharmaceutical implants containing bioactive peptides)
IT 144743-92-0D, Teverelix, salts
(pharmaceutical implants containing bioactive peptides)
RN 144743-92-0 USPATFULL
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L22 ANSWER 5 OF 8 USPATFULL on STN

AN 2000:77041 USPATFULL

TI Process to manufacture implants containing bioactive peptides

IN Deghenghi, Romano, Cheseaux Dessus B1, St. Cergue, Switzerland

PI US 6077523 20000620

AI US 1999-311744 19990514 (9)

RLI Division of Ser. No. US 1997-897942, filed on 21 Jul 1997, now patented,
Pat. No. US 5945128

PRAI US 1996-25444P 19960904 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Azpuru, Carlos A.

LREP Pennie & Edmonds LLP

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 353

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical implant for the delivery of an effective amount of a bioactive peptide or peptide analog over a period of 1 to 12 months. This implant has a diameter of about 1 to 2 mm, a length of between about 10 and 25 mm and is obtainable from a process which includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 μ m; sterilizing the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing

γ -radiation; wetting the ground and sterilized copolymer with a sterile aqueous slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixture of the copolymer and between about 10 and 50% of the bioactive peptide or peptide analog; drying the mixture at reduced pressure and at temperature not exceeding 25° C.; aseptically extruding the dried mixture at a temperature between about 70 and 110° C.; and aseptically cutting a cylindrical rod from the extruded mixture to form the pharmaceutical implant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0D, *Teverelix*, salts

(pharmaceutical implants containing bioactive peptides)

IT 144743-92-0D, *Teverelix*, salts

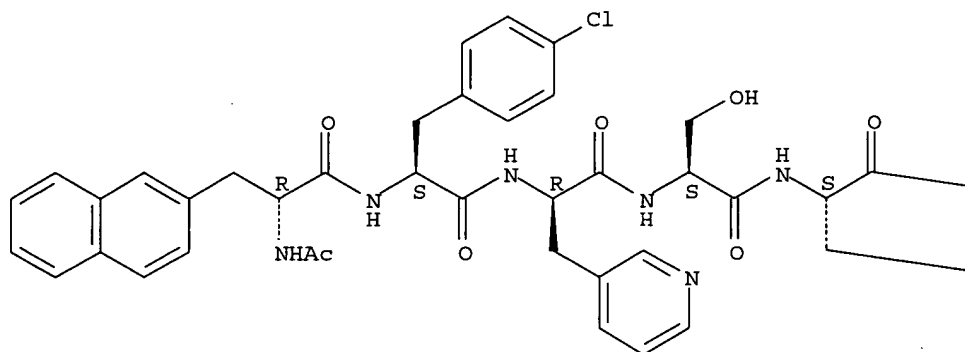
(pharmaceutical implants containing bioactive peptides)

RN 144743-92-0 USPATFULL

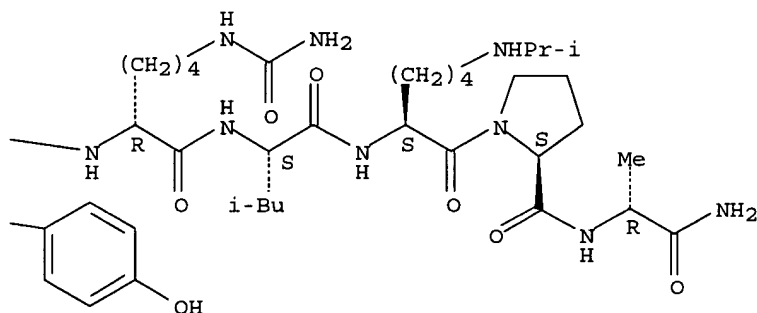
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L22 ANSWER 6 OF 8 USPATFULL on STN

AN 1999:102518 USPATFULL

TI Process to manufacture implants containing bioactive peptides

IN Deghenghi, Romano, Cheseaux Dessus B1, St. Cergue, Switzerland

PI US 5945128 19990831
 AI US 1997-897942 19970721 (8)
 PRAI US 1996-25449P 19960904 (60)
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Azpuru, Carlos A.
 LREP Pennie & Edmonds LLP
 CLMN Number of Claims: 10
 ECL Exemplary Claim: 1
 DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
 LN.CNT 326

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

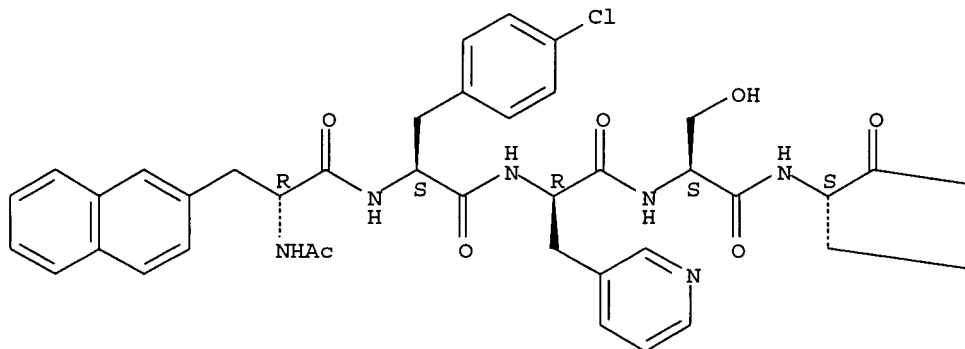
AB A process for manufacturing a pharmaceutical composition for the delivery of an effective amount of a bioactive peptide or peptide analog over a period of 1 to 12 months. This process includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 μm ; sterilizing the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing γ -radiation; wetting the ground and sterilized copolymer with a sterile aqueous slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixture of the copolymer and between about 10 and 50% of the bioactive peptide or peptide analog; drying the mixture at reduced pressure and at temperature not exceeding 25° C.; aseptically extruding the dried mixture at a temperature between about 70 and 110° C.; and aseptically cutting cylindrical rods of about 1 to 2 mm diameter and between about 10 and 25 mm in length from the extruded mixture to form the pharmaceutical implants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0D, Teverelix, salts
 (pharmaceutical implants containing bioactive peptides)
 IT 144743-92-0D, Teverelix, salts
 (pharmaceutical implants containing bioactive peptides)
 RN 144743-92-0 USPATFULL
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



AN 2002:344416 USPAT2

IN Damm, Michael, Rodemark, GERMANY, FEDERAL REPUBLIC OF

Salonek, Waldemar, Heidelberg, GERMANY, FEDERAL REPUBLIC OF

Engel, Jurgen, Alzenau, GERMANY, FEDERAL REPUBLIC OF

Bauer, Horst. Hersbruck. GERMANY. FEDERAL REPUBLIC OF

Stach, Gabriele, Frankfurt, GERMANY, FEDERAL REPUBLIC OF

PA Zentaris GmbH, Frankfurt, GERMANY, FEDERAL REPUBLIC OF

(non-U.S. corporation)

PI US 6780972 B2 20040824

AI US 2001-939532 20010824 (9)

PRAI DE 2000-10040700 20000817

DT Utility

FS GRANTED

EXNAM Primary Examiner: Brumback, Brenda; Assistant Examiner: Gupta, Anish

LREP Goodwin Procter LLP

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

DRWN 1 Drawing Figure(s); 1 Drawing Page(s)

LN.CNT 213

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for producing peptide salts, including reacting an acid addition salt of a basic starting peptide in the presence of a diluent in a mixed bed ion exchanger, with a mixture of an acid and a basic ion exchanger during the formation of a free basic peptide, and then separating the ion exchanger and then the free basic peptide, with an inorganic or organic acid, and then forming the desired acid addition salt of the peptide, and removing the diluent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, Teverelix

(method for producing peptide salts, use, and pharmaceutical preps.
containing peptide salts in relation to cetorelix embonate)

IT 144743-92-0, Teverelix

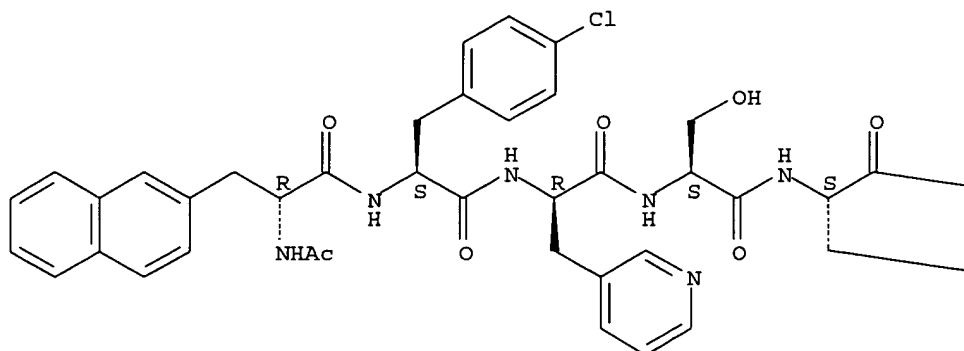
(method for producing peptide salts, use, and pharmaceutical preps.
containing peptide salts in relation to cetrorelix embonate)

RN 144743-92-0 USPAT2

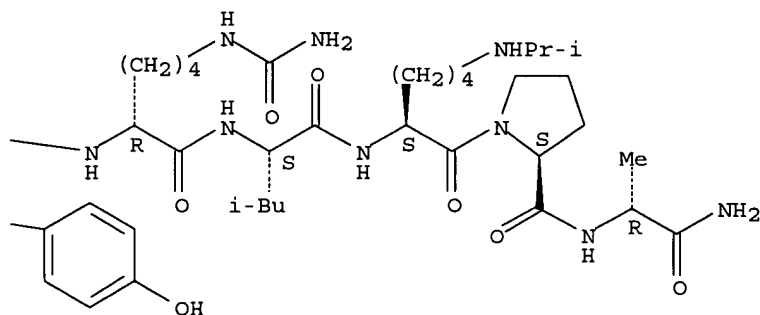
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L22 ANSWER 8 OF 8 USPAT2 on STN

AN 2001:170756 USPAT2

TI Compressed microparticles for dry injection

IN Boutignon, Francois, Ermont, FRANCE

PA Ardana Bioscience Limited, Edinburgh, UNITED KINGDOM (non-U.S. corporation)

PI US 6627600 B2 20030930

AI US 2001-764111 20010119 (9)

RLI Continuation-in-part of Ser. No. US 2000-491978, filed on 27 Jan 2000, now abandoned

DT Utility

FS GRANTED

EXNAM Primary Examiner: Hartley, Michael G.; Assistant Examiner: Choi, Frank

LREP Winston & Strawn LLP

CLMN Number of Claims: 41

ECL Exemplary Claim: 1

DRWN 10 Drawing Figure(s); 9 Drawing Page(s)

LN.CNT 958

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a pharmaceutical implant for controllably releasing a drug in a subject and methods for manufacturing and administering the implant. The implant is made of associated microparticles of a drug dispersed in a biodegradable polymer. The microparticles are sufficiently associated so that the implant maintains a predetermined shape but are not fused together so as to form a single monolithic structure. The drug can be controllably released in a subject by administration of the pharmaceutical implant without the need of a

suspending fluid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**
(compressed microparticles for dry injection)

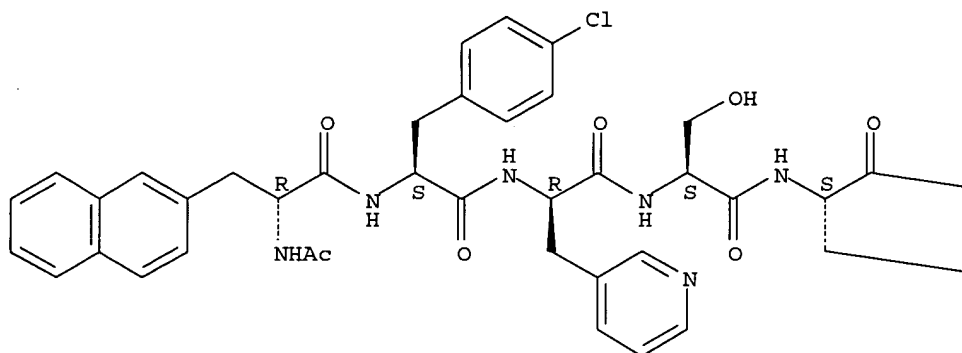
IT 144743-92-0, **Teverelix**
(compressed microparticles for dry injection)

RN 144743-92-0 USPAT2

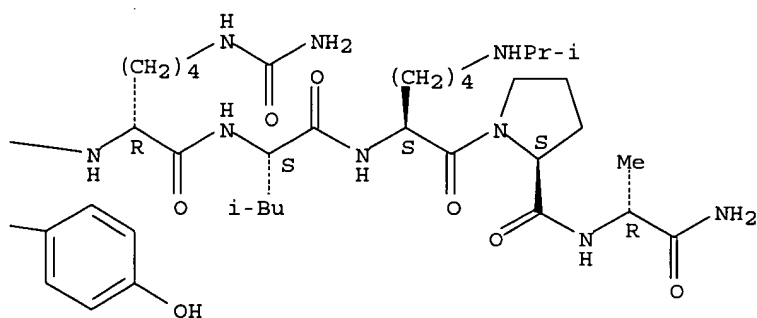
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=> d bib abs hitrn fhitr l24 tot

L24 ANSWER 1 OF 23 USPATFULL on STN

AN 2005:183941 USPATFULL

TI Pharmaceutical administration form for peptides, process for its preparation, and use

IN Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
Damm, Michael, Rodermark, GERMANY, FEDERAL REPUBLIC OF
Sarlikiotis, Werner, Peania, GREECE

PI US 2005159335 A1 20050721

AI US 2005-28875 A1 20050104 (11)

RLI Division of Ser. No. US 2001-861009, filed on 18 May 2001, PENDING
 PRAI DE 2000-10024451 20000518 <--
 DT Utility
 FS APPLICATION
 LREP GOODWIN PROCTER L.L.P, 103 EISENHOWER PARKWAY, ROSELAND, NJ, 07068, US
 CLMN Number of Claims: 26
 ECL Exemplary Claim: 1-17
 DRWN No Drawings
 LN.CNT 689

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for preventing aggregation of an LHRH antagonist in a pharmaceutical composition. The method comprises combining the LHRH antagonist in the form of an acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate or phosphate salt at least one of the acids for forming the salts in free acid form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 151272-78-5, Antarelix
 (formulation of parenteral peptide drugs to prevent aggregation)

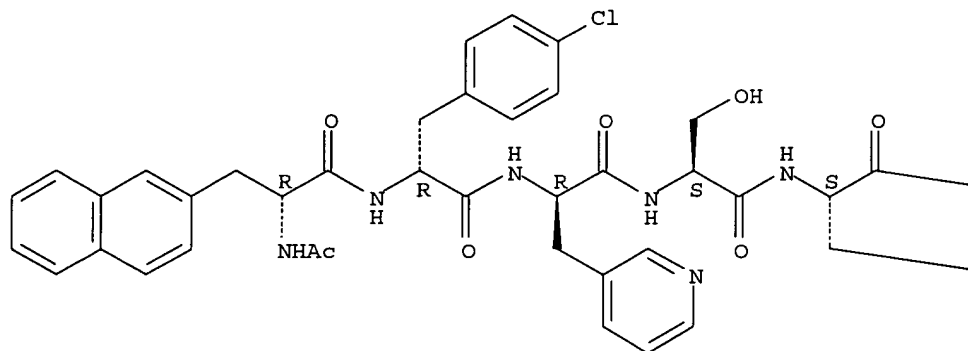
IT 151272-78-5, Antarelix
 (formulation of parenteral peptide drugs to prevent aggregation)

RN 151272-78-5 USPATFULL

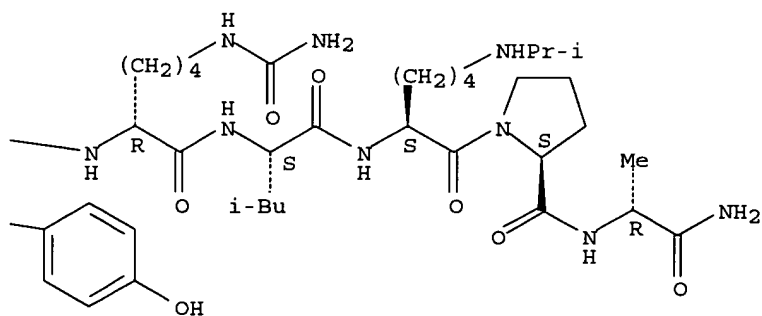
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

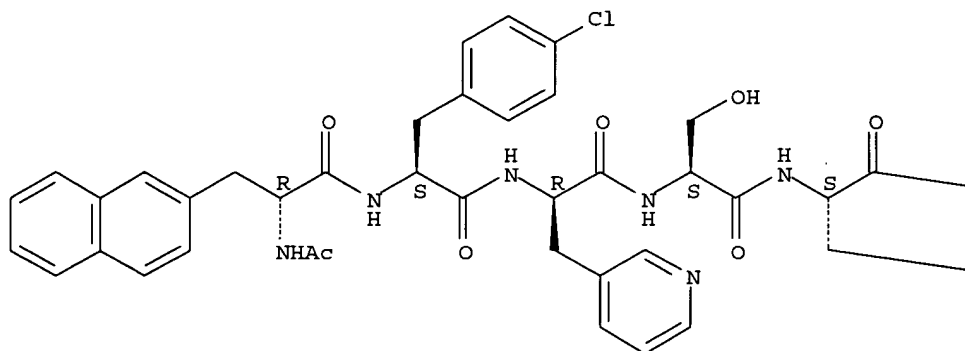


PAGE 1-B

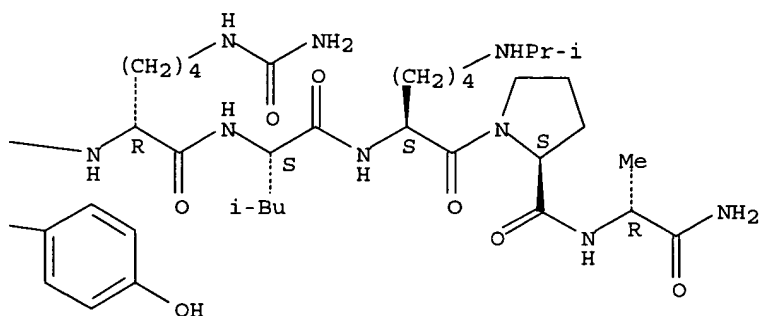


L24 ANSWER 2 OF 23 USPATFULL on STN
 AN 2005:167632 USPATFULL
 TI Bioimplant formulation
 IN Trigg, Timothy Elliot, Warrawee, AUSTRALIA
 Walsh, John Desmond, Curl Curl, AUSTRALIA
 Rathjen, Deborah Ann, Thornleigh, AUSTRALIA
 PA Peptech Limited, New South Wales, AUSTRALIA (non-U.S. corporation)
 PI US 6913761 B1 20050705
 WO 2000004897 20000203 <--
 AI US 2001-743059 19990720 (9) <--
 WO 1999-AU585 19990720 <--
 20010104 PCT 371 date
 PRAI AU 2001-4730 19980720 <--
 AU 2001-4731 19980720 <--
 AU 2001-324 19990513 <--
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: Azpuru, Carlos A.
 LREP Nixon & Vanderhye
 CLMN Number of Claims: 40
 ECL Exemplary Claim: 1
 DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
 LN.CNT 749
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB A pharmaceutical and/or veterinary formulation comprising about 2-30%
 (w/w) (on an active basis) of at least one active agent, about 0.5-20.0%
 (w/w) of a pore-foaming agent and the balance stearin. Such formulations
 provided release of the at least one active agent in humans and other
 animals for periods of 7 days up to about 2 years.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 IT 144743-92-0, **Teverelix**
 (bioimplant formulations containing stearin)
 IT 144743-92-0, **Teverelix**
 (bioimplant formulations containing stearin)
 RN 144743-92-0 USPATFULL
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-
 phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-
 (aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-
 (9CI) (CA INDEX NAME)
 Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 3 OF 23 USPATFULL on STN

AN 2005:17275 USPATFULL

TI Solid peptide preparations for inhalation and their preparation

IN Lizio, Rosario, Buttelborn, GERMANY, FEDERAL REPUBLIC OF

Damm, Michael, Rodermark, GERMANY, FEDERAL REPUBLIC OF

Sarlikiotis, Werner, Peania, GREECE

Wolf-Heuss, Elisabeth, Mosbach, GERMANY, FEDERAL REPUBLIC OF

PI US 2005014677 A1 20050120

AI US 2004-808239 A1 20040323 (10)

RLI Continuation of Ser. No. US 2001-944060, filed on 31 Aug 2001, ABANDONED

PRAI DE 2000-10043509 20000901 <--

DT Utility

FS APPLICATION

LREP GOODWIN PROCTER L.L.P, 103 EISENHOWER PARKWAY, ROSELAND, NJ, 07068

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 731

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to solid pharmaceutical preparations, in particular for inhalatory administration in mammals, their preparation and their use such as, for example, in powder inhalers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**
(solid peptide preps. for inhalation and production)

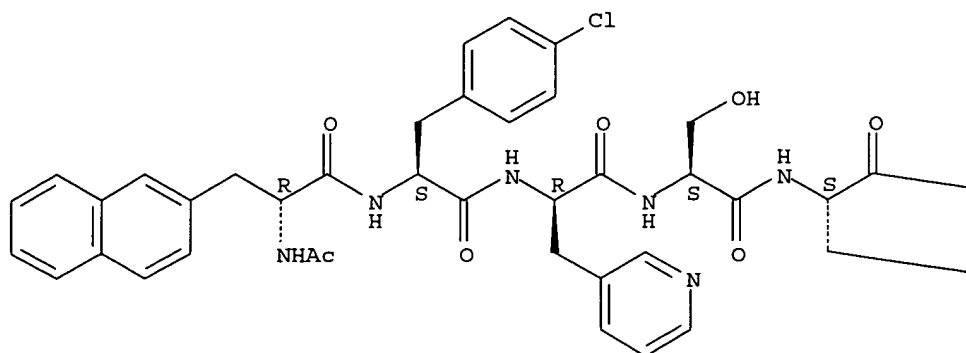
IT 144743-92-0, **Teverelix**
(solid peptide preps. for inhalation and production)

RN 144743-92-0 USPATFULL

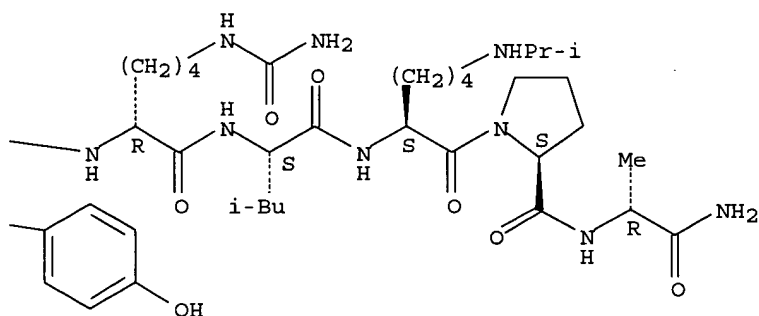
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 4 OF 23 USPATFULL on STN

AN 2004:327976 USPATFULL

TI Method for the synthesis of peptide salts, their use and pharmaceutical preparations containing the peptide salts

IN Damm, Michael, Rodemark, GERMANY, FEDERAL REPUBLIC OF
 Salonek, Waldemar, Heidelberg, GERMANY, FEDERAL REPUBLIC OF
 Engel, Jurgen, Alzenau, GERMANY, FEDERAL REPUBLIC OF
 Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
 Stach, Gabriele, Frankfurt, GERMANY, FEDERAL REPUBLIC OF

PI US 2004259801 A1 20041223

AI US 2004-895468 A1 20040713 (10)

RLI Continuation of Ser. No. US 2001-939532, filed on 24 Aug 2001, GRANTED,
 Pat. No. US 6780972

PRAI DE 2000-10040700 20000817

<--

DT Utility

FS APPLICATION

LREP GOODWIN PROCTER L.L.P., 103 EISENHOWER PARKWAY, ROSELAND, NJ, 07068

CLMN Number of Claims: 27

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 283

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition comprising a peptide salt having a pharmaceutically acceptable anion prepared by the method comprising the steps of: contacting a first peptide salt with a diluent to form a diluent solution; contacting the diluent solution containing the first peptide

salt with a mixed bed ion exchanger, wherein the mixed bed ion exchanger has strongly acidic cations and strong anion exchangers; separating the mixed bed ion exchanger from the diluent solution; contacting the diluent solution with an acid having a pharmaceutically acceptable anion, thereby forming an acid addition salt of the peptide having the pharmaceutically acceptable anion; adding an adjuvant to the diluent solution; and separating the diluent from the diluent solution. The invention also relates to a method for treatment of benign prostate hyperplasia, myoma, or endometriosis with the composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**

(method for producing peptide salts, use, and pharmaceutical preps. containing peptide salts in relation to cetrorelix embonate)

IT 144743-92-0, **Teverelix**

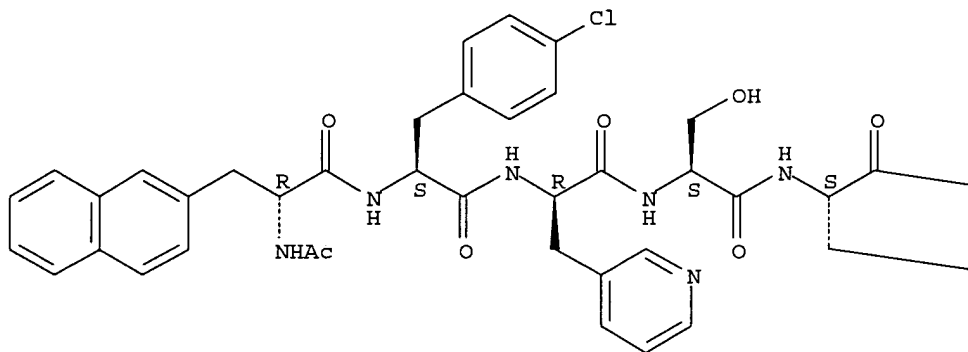
(method for producing peptide salts, use, and pharmaceutical preps. containing peptide salts in relation to cetrorelix embonate)

RN 144743-92-0 USPATFULL

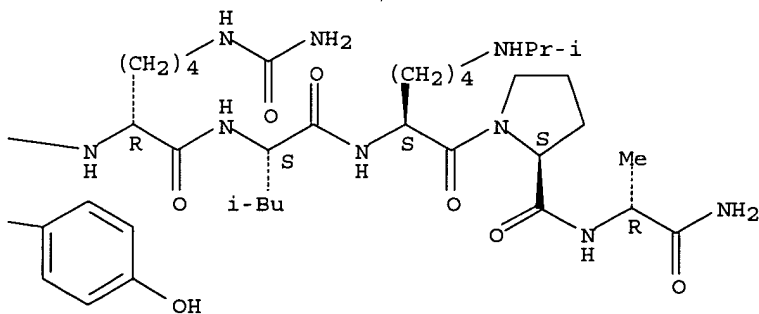
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 5 OF 23 USPATFULL on STN
AN 2004:178968 USPATFULL

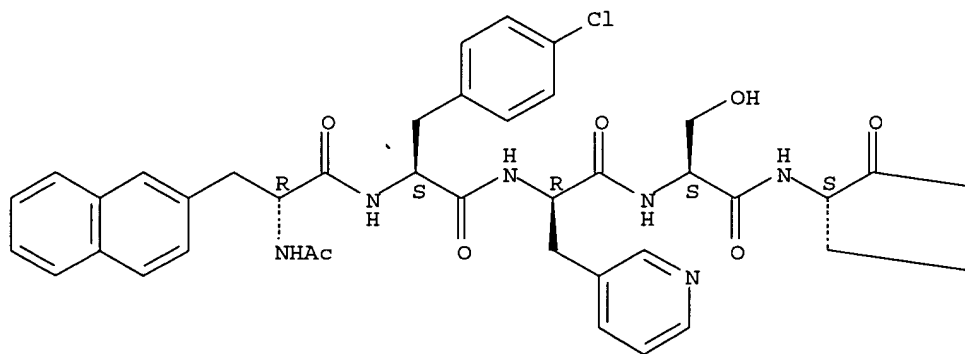
TI Use of LHRH-antagonists in doses that do not cause castration for the improvement of T-cell mediated immunity
IN Engel, Jorgen, Alezenau, GERMANY, FEDERAL REPUBLIC OF
Peukert, Manfred, Oberursel, GERMANY, FEDERAL REPUBLIC OF
PI US 2004138138 A1 20040715
AI US 2002-748887 A1 20020730 (10)
PRAI US 2001-309735P 20010802 (60) <--
DT Utility
FS APPLICATION
LREP Goodwin Procter LLP, 599 Lexington Avenue, New York, NY, 10022
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 95
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns the use of appropriate doses of an LHRH-antagonist to lower sex hormone levels resulting in a modification of the T-cell population in an individual suffering from a disease that will respond favourably to such modification. A preferred LHRH-antagonist is cetrorelix.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

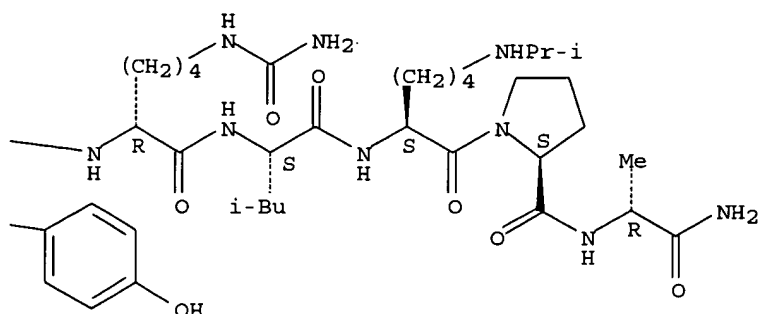
IT 144743-92-0, Teverelix
(LHRH antagonists in non-castrating doses for improvement of T-cell-mediated immunity)
IT 144743-92-0, Teverelix
(LHRH antagonists in non-castrating doses for improvement of T-cell-mediated immunity)
RN 144743-92-0 USPTAFULL
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 6 OF 23 USPATFULL on STN

AN 2004:121167 USPATFULL

TI Treatment for inhibiting neoplastic lesions

IN Shanahan-Prendergast, Elizabeth, County Kildare, IRELAND

PI US 2004092583 A1 20040513

AI US 2004-250535 A1 20040102 (10)

WO 2002-IE1 20020102

PRAI IE 2001-20010002 20010102 <--

DT Utility

FS APPLICATION

LREP HOFFMANN & BARON, LLP, 6900 JERICHO TURNPIKE, SYOSSET, NY, 11791

CLMN Number of Claims: 69

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2329

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention discloses the use of incensole and/or furanogermacrens, derivatives metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compounds can be administered alone or in combination with conventional chemotherapeutic, anti-rival, anti-parasite agents, radiation and/or surgery.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 151272-78-5, Antarelix
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

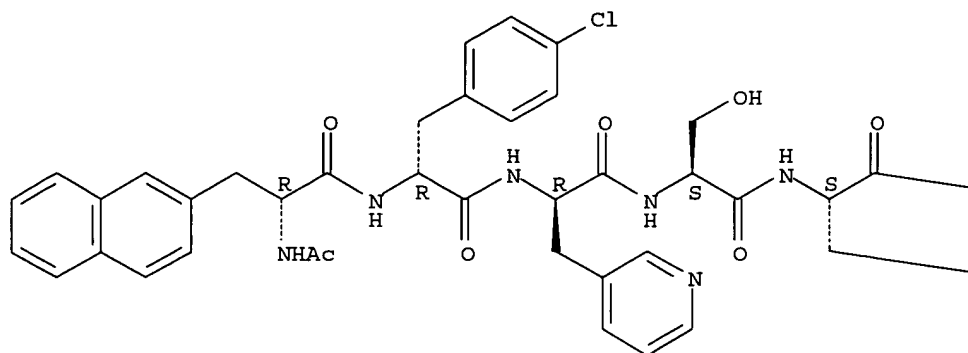
IT 151272-78-5, Antarelix
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

RN 151272-78-5 USPATFULL

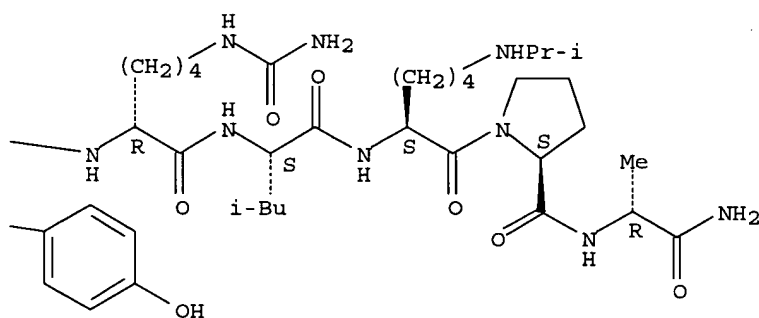
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 7 OF 23 USPATFULL on STN

AN 2004:57931 USPATFULL

TI Combination therapy for estrogen-dependent disorders

IN Purandare, Dinesh, Branchburg, NJ, UNITED STATES

PI US 2004043938 A1 20040304

AI US 2003-416844 A1 20030912 (10)

<--

WO 2001-US43847 20011106

<--

DT Utility

FS APPLICATION

LREP MCDONNELL BOEHNNEN HULBERT & BERGHOFF, 300 SOUTH WACKER DRIVE, SUITE 3200, CHICAGO, IL, 60606

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 449

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a combination therapy for treating estrogen dependent cancers in susceptible mammals, including humans, comprising the steps of inhibiting hormone output of their testis or ovaries, respectively, and administering to said mammal at least one aromatase inhibitor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, Teverelix

(aromatase inhibitor combination with inhibition of testicular and ovarian hormone output for treatment of estrogen-dependent cancers)

IT 144743-92-0, Teverelix

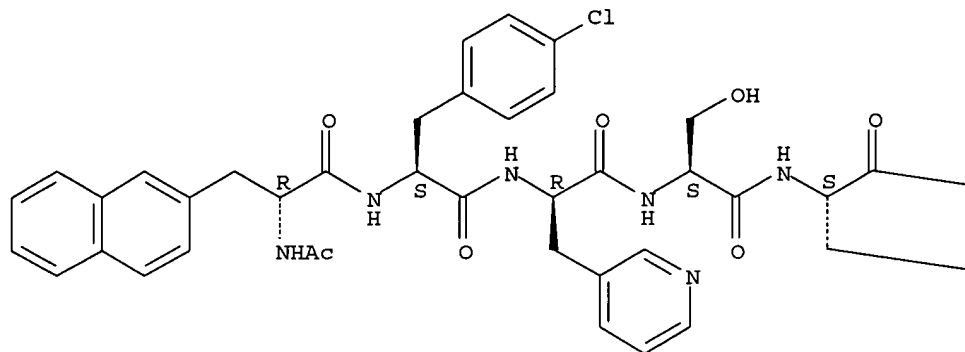
(aromatase inhibitor combination with inhibition of testicular and ovarian hormone output for treatment of estrogen-dependent cancers)

RN 144743-92-0 USPATFULL

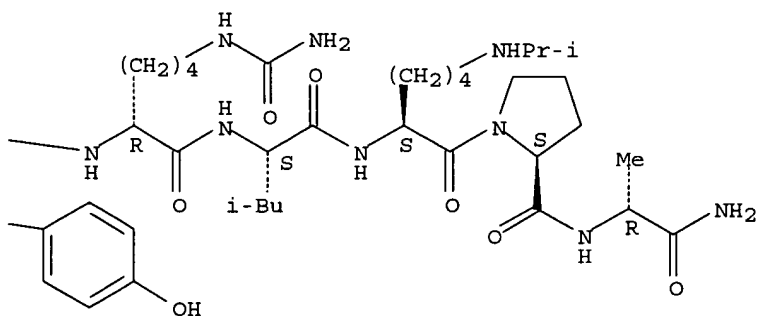
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 8 OF 23 USPATFULL on STN

AN 2003:251571 USPATFULL

TI Medicinal preparations for treating sex hormone-dependent diseases

IN Igari, Yasutaka, Hyogo, JAPAN

Kamei, Shigeru, Hyogo, JAPAN

PI US 2003176360 A1 20030918

AI US 2003-312998 A1 20030102 (10)

WO 2001-JP5808 20010704

PRAI JP 2000-208253 20000705

DT Utility

FS APPLICATION

LREP TAKEDA PHARMACEUTICALS NORTH AMERICA, INC, INTELLECTUAL PROPERTY DEPARTMENT, 475 HALF DAY ROAD, SUITE 500, LINCOLNSHIRE, IL, 60069

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1439

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Medicinal preparations for treating sex hormone-dependent diseases which comprise a combination of a compound having a luteinizing hormone-releasing hormone agonistic effect or its salt with a compound having a luteinizing hormone-releasing hormone antagonistic effect or its salt for administering the compound having a luteinizing hormone-releasing hormone agonistic effect or its salt followed by the compound having a luteinizing hormone-releasing hormone antagonistic effect or its salt. By using these preparations, the concentration of a sex hormone (for example, testosterone, LH, FSH, estrogen) can be quickly recovered after the medicable period of a compound having a luteinizing hormone-releasing hormone antagonistic effect or its salt or a preparation containing the same (preferably a sustained-release preparation), which makes it possible to definitely determine the drug cessation period in an intermittent treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 151272-78-5, Antarelix

(use of LHRH agonists and antagonists for intermittent treatment of sex hormone-dependent diseases)

IT 151272-78-5, Antarelix

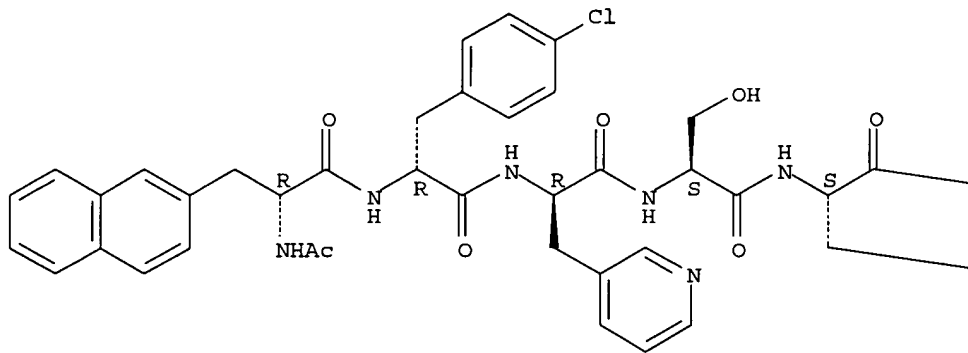
(use of LHRH agonists and antagonists for intermittent treatment of sex hormone-dependent diseases)

RN 151272-78-5 USPATFULL

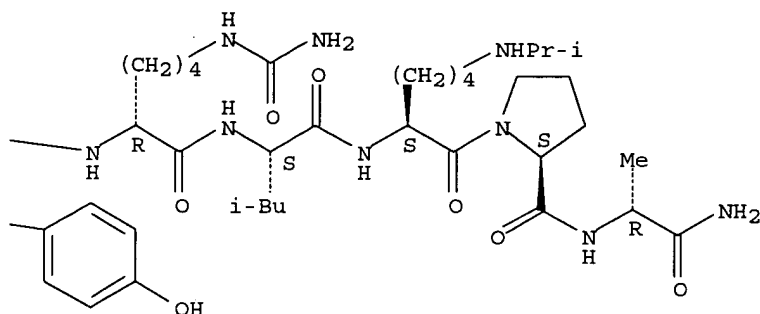
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 9 OF 23 USPATFULL on STN

AN 2003:146762 USPATFULL

TI Injectable solution of an LHRH antagonist

IN Sarlikiotis, Werner, Peania, GERMANY, FEDERAL REPUBLIC OF
 Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
 Rischer, Matthias, Frankfurt a.M., GERMANY, FEDERAL REPUBLIC OF
 Engel, Jorgen, Alzenau, GERMANY, FEDERAL REPUBLIC OF

PI US 2003100509 A1 20030529

AI US 2002-279625 A1 20021023 (10)

PRAI US 2001-333662P 20011127 (60) <--

DT Utility

FS APPLICATION

LREP GOODWIN PROCTER L.L.P., 7 BECKER FARM ROAD, ROSELAND, NJ, 07068

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 183

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An aqueous injectable solution of an LHRH antagonist, such as Cetrorelix,
 in an organic, pharmaceutically acceptable acid, such as gluconic acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**
 (injectable solution of an LHRH antagonist)

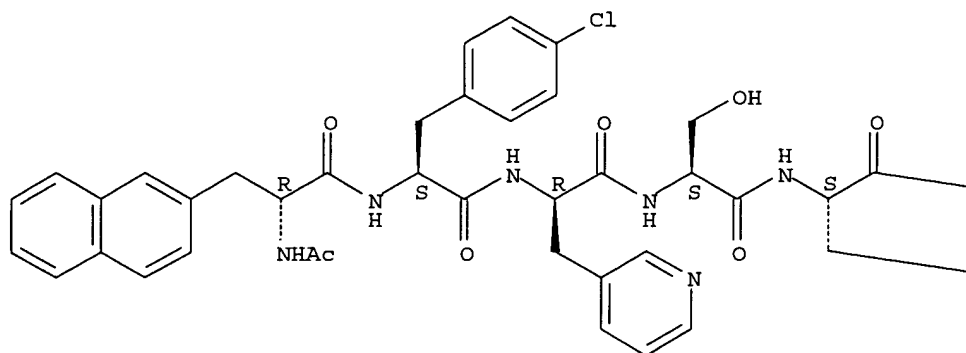
IT 144743-92-0, **Teverelix**
 (injectable solution of an LHRH antagonist)

RN 144743-92-0 USPATFULL

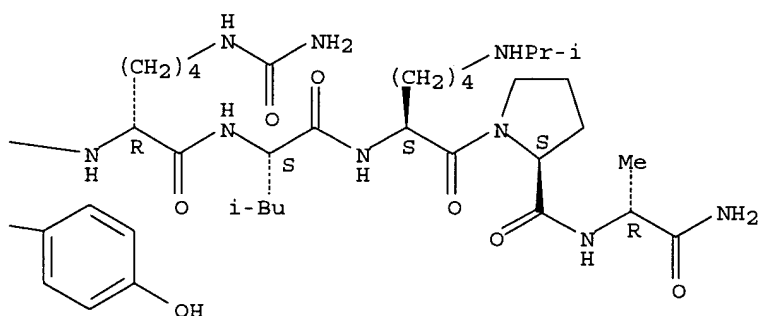
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-
 phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-
 (aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 10 OF 23 USPATFULL on STN

AN 2002:344416 USPATFULL

TI Method for the synthesis of peptide salts, their use and the pharmaceutical preparations, containing peptide salts

IN Damm, Michael, Rodemark, GERMANY, FEDERAL REPUBLIC OF
 Salonek, Waldemar, Heidelberg, GERMANY, FEDERAL REPUBLIC OF
 Engel, Jurgen, Alzenau, GERMANY, FEDERAL REPUBLIC OF
 Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
 Stach, Gabriele, Frankfurt, GERMANY, FEDERAL REPUBLIC OF

PI US 2002198146 A1 20021226

US 6780972 B2 20040824

AI US 2001-939532 A1 20010824 (9)

PRAI DE 2000-10040700 20000817

DT Utility

FS APPLICATION

LREP GABRIEL P. KATONA, GOODWIN PROCTER LLP, 599 LEXINGTON AVE. 40TH FL, NEW
 YORK, NY, 10022

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN 1 Drawing Page(s)

LN.CNT 215

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for producing peptide salts, including reacting an acid
 addition salt of a basic starting peptide in the presence of a diluent
 in a mixed bed ion exchanger, with a mixture of an acid and a basic ion
 exchanger during the formation of a free basic peptide, and then

separating the ion exchanger and then the free basic peptide, with an inorganic or organic acid, and then forming the desired acid addition salt of the peptide, and removing the diluent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**

(method for producing peptide salts, use, and pharmaceutical preps. containing peptide salts in relation to cetrorelix embonate)

IT 144743-92-0, **Teverelix**

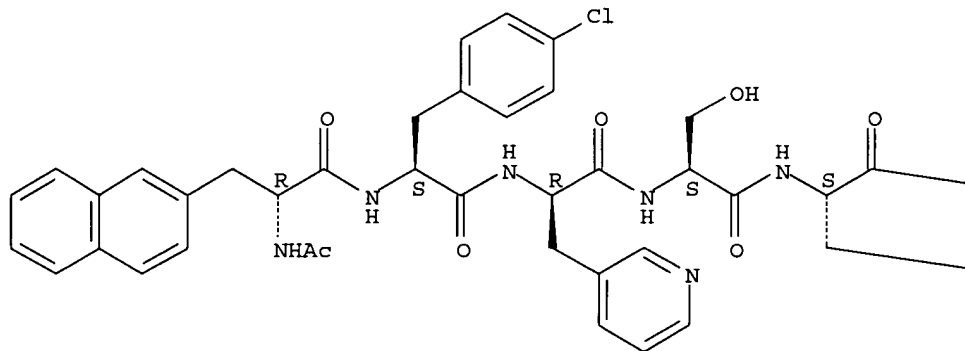
(method for producing peptide salts, use, and pharmaceutical preps. containing peptide salts in relation to cetrorelix embonate)

RN 144743-92-0 USPATFULL

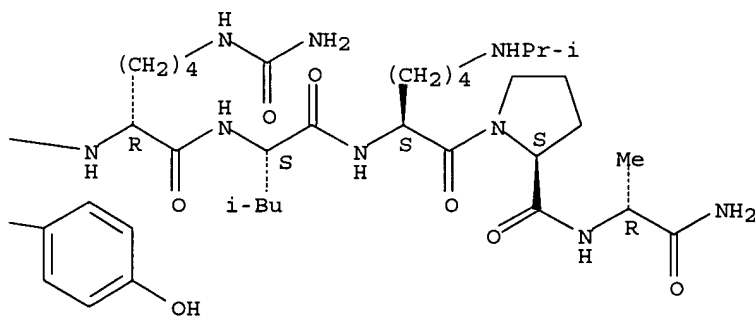
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 11 OF 23 USPATFULL on STN

AN 2002:315074 USPATFULL

TI Treatment of dementia and neurodegenerative diseases with intermediate doses of LHRH antagonists

IN Engel, Jurgén, Alzenau, GERMANY, FEDERAL REPUBLIC OF
Voegeli, Rainer, Biebergemund-Bieber, GERMANY, FEDERAL REPUBLIC OF

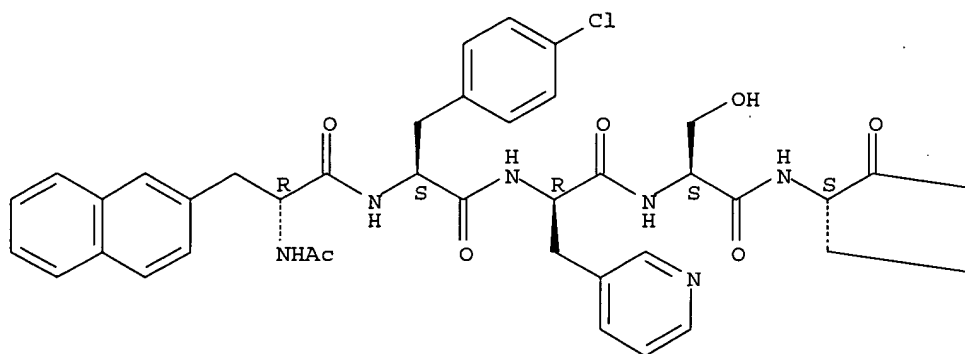
PI US 2002177556 A1 20021128

AI US 2002-133967 A1 20020427 (10)

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Absolute stereochemistry.

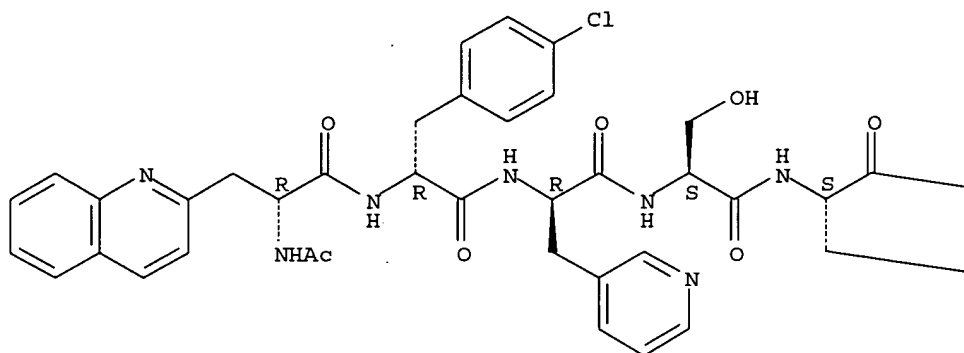
PAGE 1-A



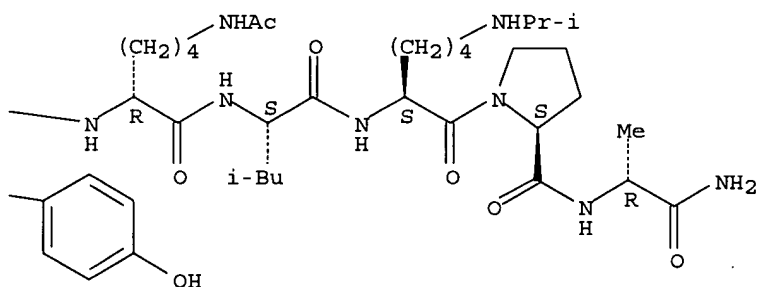
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21/11/2005

PAGE 1-A

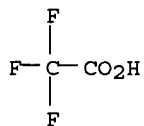


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L24 ANSWER 13 OF 23 USPATFULL on STN

AN 2002:227675 USPATFULL

TI Solid peptide preparations for inhalation and their preparation

IN Lizio, Rosario, Buttelborn, GERMANY, FEDERAL REPUBLIC OF

Damm, Michael, Rodermark, GERMANY, FEDERAL REPUBLIC OF

Sarlikiotis, Werner, Peania, GREECE

Wolf-Heuss, Elisabeth, Mosbach, GERMANY, FEDERAL REPUBLIC OF

PI US 2002122826 A1 20020905

AI US 2001-944060 A1 20010831 (9)

PRAI DE 2000-10043509 20000901

DT Utility

FS APPLICATION

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LREP Goodwin Procter L.L.P., 599 Lexington Avenue, 40th floor, New York, NY,
10022
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 764

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to solid pharmaceutical preparations, in particular for inhalatory administration in mammals, their preparation and their use such as, for example, in powder inhalers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 144743-92-0, **Teverelix**
(solid peptide preps. for inhalation and production)

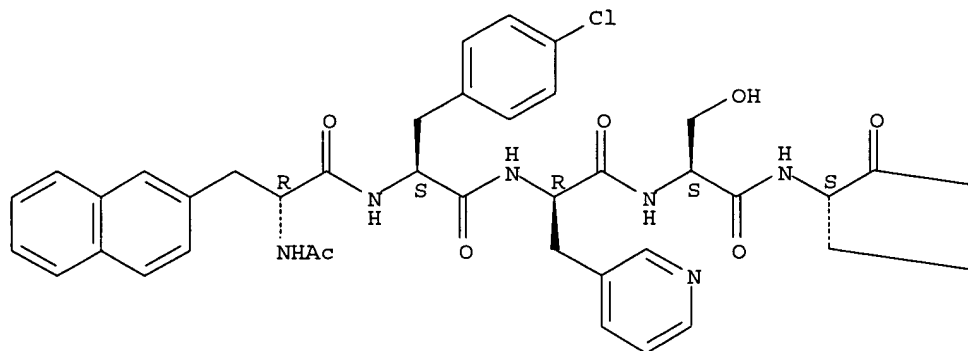
IT 144743-92-0, **Teverelix**
(solid peptide preps. for inhalation and production)

RN 144743-92-0 USPATFULL

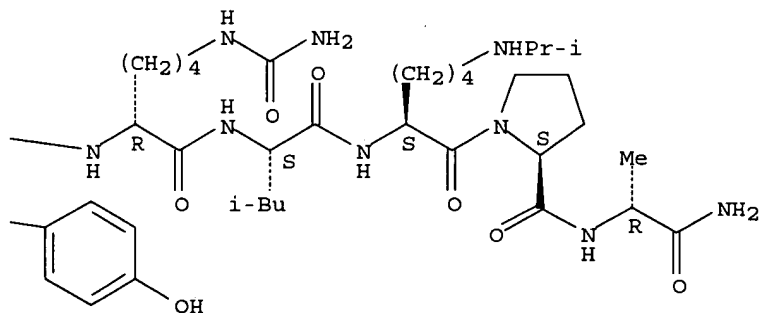
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-L-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 14 OF 23 USPATFULL on STN
AN 2002:214228 USPATFULL
TI Novel inhibitor of beta amyloid cleavage enzyme

IN Boyd, James G., Mystic, CT, UNITED STATES
 Singleton, David H., Noank, CT, UNITED STATES
 PA Pfizer Inc. (U.S. corporation)
 PI US 2002115616 A1 20020822
 AI US 2002-75686 A1 20020214 (10)
 PRAI US 2001-270006P 20010220 (60) <--
 DT Utility
 FS APPLICATION
 LREP PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY,
 10017-5612
 CLMN Number of Claims: 15
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 576

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to a novel inhibitor of beta amyloid cleavage enzyme (BACE, transmembrane aspartyl protease beta-secretase, beta site APP cleavage enzyme, memapsin-2, BACE-1), pharmaceutical compositions containing it and its use in the treatment of neurological disorders such as Alzheimer's disease, Crutzfield-Jacob's disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stroke, down's syndrome, pancreatitis, inclusion body myocytis, other peripheral amyloidoses and diabetes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186836-91-9P
 (LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)

IT 186836-91-9P
 (LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)

RN 186836-91-9 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-acetyl-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, mono(trifluoroacetate) (salt) (9CI)
 (CA INDEX NAME)

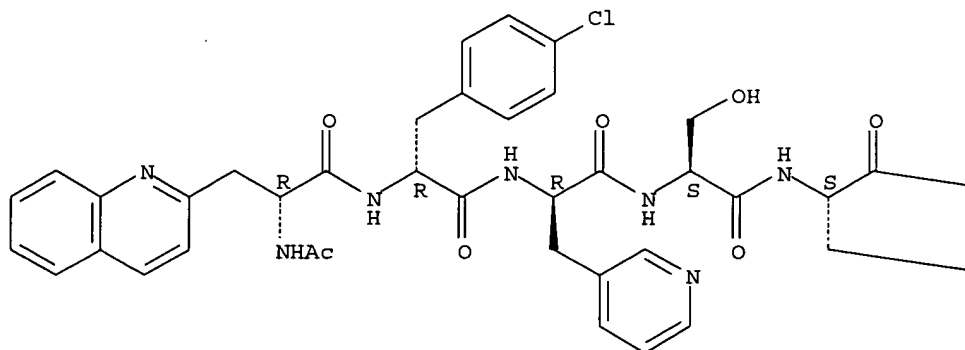
CM 1

CRN 186836-90-8

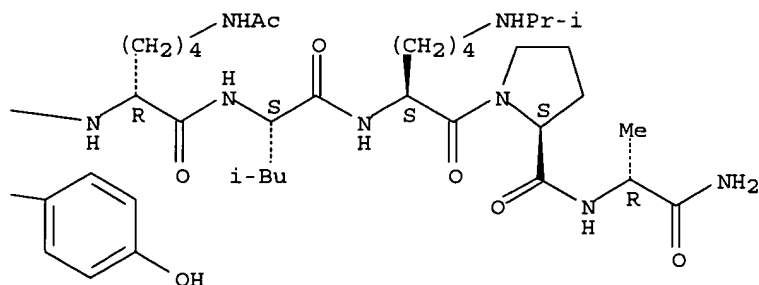
CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A



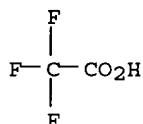
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L24 ANSWER 15 OF 23 USPATFULL on STN
 AN 2002:181669 USPATFULL
 TI LHRH antagonist peptides
 IN Roeske, Roger W., Indianapolis, IN, United States
 PA Advanced Research & Technology Institute, Indianapolis, IN, United States (U.S. corporation)
 PI US 6423686 B1 20020723
 US 2002115615 A1 20020822
 WO 9640757 19961219 <--
 AI US 1998-973378 19980406 (8) <--
 WO 1996-US9852 19960607 <--
 19980406 PCT 371 date
 RLI Continuation of Ser. No. US 1995-480494, filed on 7 Jun 1995, now patented, Pat. No. US 5843901
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: Borin, Michael
 LREP Lahive & Cockfield LLP, DeConti, Jr., Giulio A., Laccotripe, Maria C.
 CLMN Number of Claims: 18
 ECL Exemplary Claim: 1
 DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
 LN.CNT 1789
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Methods of treating a subject having a disorder associated with LHRH activity are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186836-91-9P

(LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)

IT 186836-91-9P

(LHRH antagonist synthetic peptide analogs with pharmaceutical

applications as cancer inhibitors or contraceptive agents)

RN 186836-91-9 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-acetyl-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, mono(trifluoroacetate) (salt) (9CI)
(CA INDEX NAME)

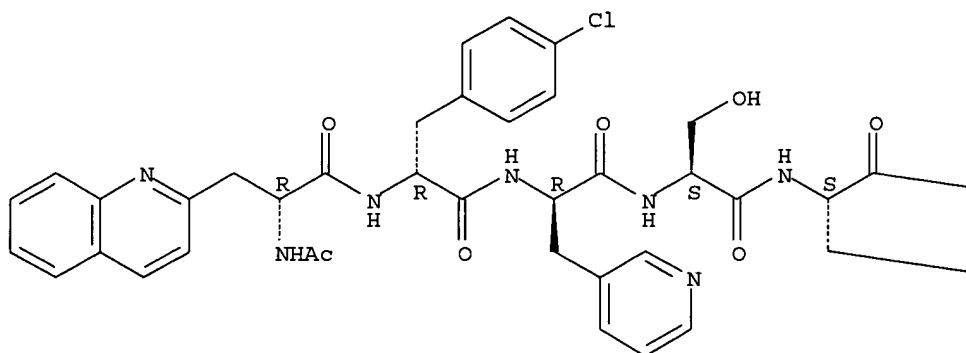
CM 1

CRN 186836-90-8

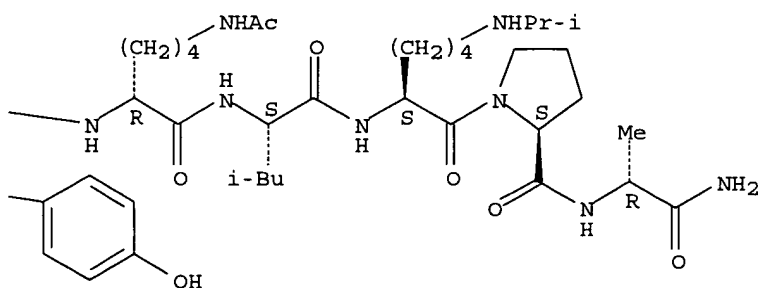
CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A



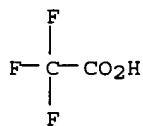
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



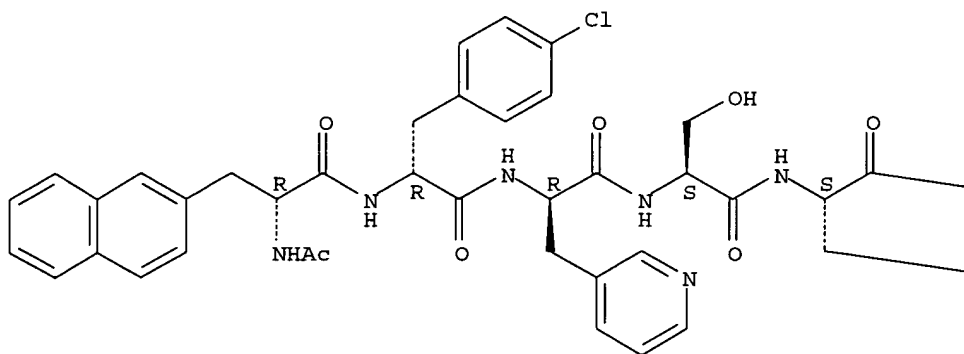
L24 ANSWER 16 OF 23 USPATFULL on STN
 AN 2002:72856 USPATFULL
 TI Pharmaceutical administration form for peptides, process for its preparation, and use
 IN Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
 Damm, Michael, Rodermark, GERMANY, FEDERAL REPUBLIC OF
 Sarlikiotis, Werner, Peania, GREECE
 PI US 2002039996 A1 20020404
 AI US 2001-861009 A1 20010518 (9) <--
 PRAI DE 2000-10024451 20000518 <--
 DT Utility
 FS APPLICATION
 LREP GABGRIEL P. KATONA L.L.P., 14th Floor, 708 Third Avenue, New York, NY, 10017
 CLMN Number of Claims: 17
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 571
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB The invention relates to pharmaceutical administration forms suitable for parenteral administration, which contains [sic] peptides prone to aggregation in the form of their acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate or phosphate salts in dissolved or dispersed form and additionally comprises [sic] one of the acids mentioned as free acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

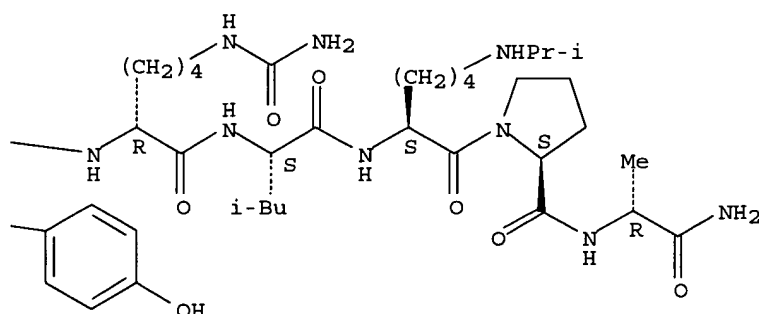
IT 151272-78-5, Antarelix
 (formulation of parenteral peptide drugs to prevent aggregation)
 IT 151272-78-5, Antarelix
 (formulation of parenteral peptide drugs to prevent aggregation)
 RN 151272-78-5 USPATFULL
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 17 OF 23 USPATFULL on STN

AN 2001:108015 USPATFULL

TI Process for the one-stage resalting and purification of oligopeptides

IN Gunther, Kurt, Staatsangehorigkeit, Germany, Federal Republic of
 Kunz, Franz-Rudolf, Staatsangehorigkeit, Germany, Federal Republic of
 Drauz, Karlheinz, Staatsangehorigkeit, Germany, Federal Republic of
 Muller, Thomas, Staatsangehorigkeit, Germany, Federal Republic of

PA Degussa-Huls Aktiengesellschaft, Germany, Federal Republic of (non-U.S.
 corporation)

PI US 6258933 B1 20010710 <--

AI US 1999-276709 19990326 (9) <--

PRAI DE 1998-19813849 19980327 <--

DT Utility

FS GRANTED

EXNAM Primary Examiner: Low, Christopher S. F.

LREP Pillsbury Madison & Sutro LLP

CLMN Number of Claims: 16

ECL Exemplary Claim: 1

DRWN 9 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 507

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a process for the one-stage resalting and purification of oligopeptides. Oligopeptides are often not formed directly as acetates when synthesised. Acetate salts of oligopeptides are however desirable as bulk-active material for medical and formulation reasons. Processes known from the prior art have hitherto involved two separate steps or pyridine-containing solvents. The resalting and purification can be combined in one step and the use of pyridine as solvent can be avoided, if the oligopeptide in the form of its chloride salt is purified with an acetate-containing solvent by liquid chromatography methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 244792-32-3P
 (method for single-stage salt formation and purification of oligopeptides)

IT 244792-28-7P 244792-29-8P
 (method for single-stage salt formation and purification of oligopeptides)

IT 244792-32-3P
 (method for single-stage salt formation and purification of oligopeptides)

RN 244792-32-3 USPATFULL

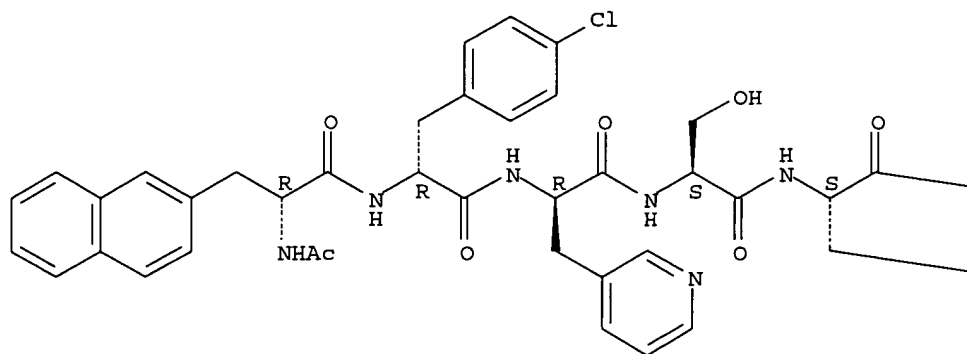
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, diacetate (salt) (9CI) (CA INDEX NAME)

CM 1

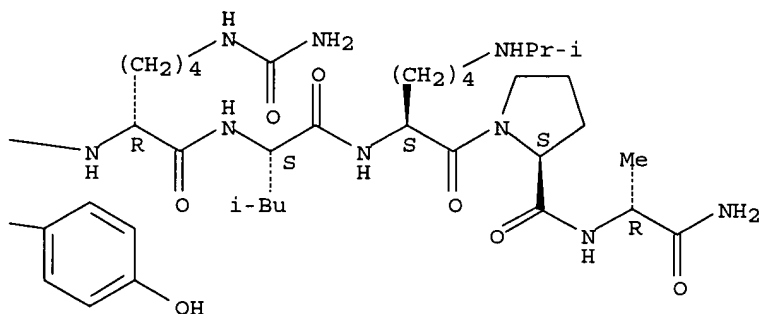
CRN 151272-78-5
 CMF C74 H100 Cl N15 O14
 CDES 5:D,D,D,D,L,L,D,L,L,L,D

Absolute stereochemistry.

PAGE 1-A

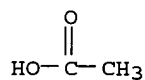


PAGE 1-B



CM 2

CRN 64-19-7
 CMF C2 H4 O2



L24 ANSWER 18 OF 23 USPATFULL on STN
 AN 2000:50805 USPATFULL
 TI Process for the preparation of immobilized and activity-stabilized
 complexes of LHRH antagonists
 IN Engel, Jurgen, Alzenau, Germany, Federal Republic of
 Deger, Wolfgang, Frankfurt, Germany, Federal Republic of
 Reissmann, Thomas, Frankfurt, Germany, Federal Republic of
 Losse, Gunter, Dresden, Germany, Federal Republic of

Naumann, Wolfgang, Zug, Germany, Federal Republic of
 Murgas, Sandra, Dresden, Germany, Federal Republic of
 PA Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of
 (non-U.S. corporation)
 PI US 6054555 20000425 <--
 AI US 1999-422990 19991022 (9) <--
 RLI Division of Ser. No. US 1998-48244, filed on 26 Mar 1998
 PRAI DE 1997-19712718 19970326 <--
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Moezie, F. T.
 LREP Pillsbury Madison & Sutro LLP
 CLMN Number of Claims: 4
 ECL Exemplary Claim: 1
 DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
 LN.CNT 263

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

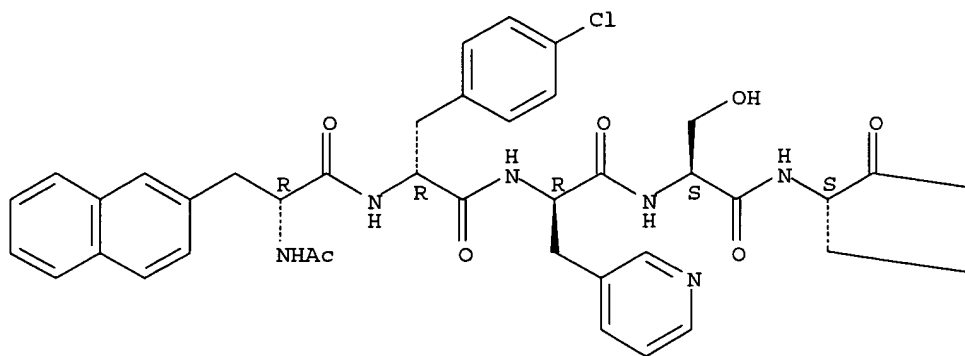
AB In this invention, a release-delaying system is to be developed for LHRH antagonists, in particular for cetrorelix, which allows the active compound to be released in a controlled manner over several weeks by complexation with suitable biophilic carriers. The acidic polyamino acids polyglutamic acid and polyaspartic acid were selected for complexation with cetrorelix. The cetrorelix polyamino acid complexes are prepared from aqueous solutions by combination of the solutions and precipitation of the complexes, which are subsequently centrifuged off and dried over P.sub.2 O.sub.5 in vacuo. If complexes having a defined composition are to be obtained, lyophilization proves to be a suitable method. The cetrorelix-carboxylic acid complexes were also prepared from the aqueous solutions. In the random liberation system, the acidic polyamino acids poly-Glu and poly-Asp showed good release-delaying properties as a function of the hydrophobicity and the molecular mass of the polyamino acid. In animal experiments, it was possible to confirm the activity of the cetrorelix-polyamino acid complexes as a depot system in principle. It is thus possible by complexation of cetrorelix with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of active compound here can be controlled by the nature and the molecular mass of the polymers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

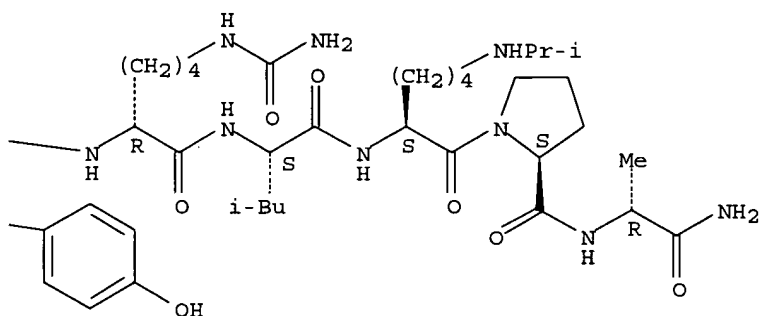
IT 151272-78-5D, Antarelix, complexes with poly(amino acids)
 (immobilized activity-stabilized LHRH antagonist complexes and their production)
 IT 151272-78-5D, Antarelix, complexes with poly(amino acids)
 (immobilized activity-stabilized LHRH antagonist complexes and their production)
 RN 151272-78-5 USPATFULL
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 19 OF 23 USPATFULL on STN

AN 2000:30970 USPATFULL

TI Method for preheating permeable, thermoformable material

IN Gupte, Sunil K., Livonia, MI, United States

PA Lear Corporation, Southfield, MI, United States (U.S. corporation)

PI US 6036896

20000314

<--

AI US 1998-82743

19980521 (9)

<--

DT Utility

FS Granted

EXNAM Primary Examiner: Silbaugh, Jan H.; Assistant Examiner: Lee, Dae Young

LREP Brooks & Kushman PC

CLMN Number of Claims: 24

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 428

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of preheating a thermoformable laminate assembly having first and second sides is disclosed. The method includes supplying pressurized heated air to first and second manifolds, each of which has an inlet for receiving the heated air and a plurality of orifices for passing the heated air out of the respective manifold. The manifolds are configured such that the orifices disposed progressively further away from the inlet of one manifold correspond with the orifices disposed progressively nearer to the inlet of the other manifold. The method further includes homogenizing the heated air and introducing the heated air onto the first side of the laminate assembly. A suction is developed

on the second side of the laminate assembly to draw the heated air through the assembly, thereby convectively heating the assembly. An apparatus for practicing the method is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 151272-78-5, Antarelix

(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)

IT 151272-78-5, Antarelix

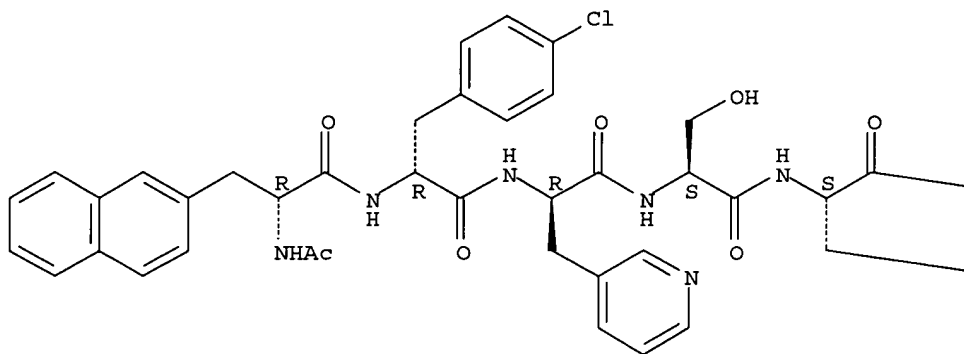
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)

RN 151272-78-5 USPATFULL

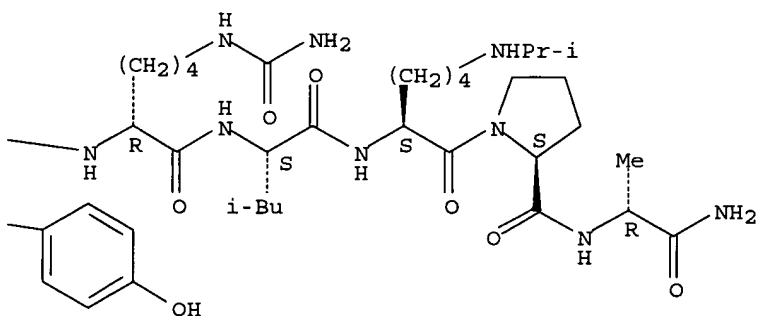
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 20 OF 23 USPATFULL on STN

AN 2000:15636 USPATFULL

TI Immobilized and activity-stabilized complexes of LHRH antagonists and processes for their preparation

IN Engel, Jurgen, Alzenau, Germany, Federal Republic of
Deger, Wolfgang, Frankfurt, Germany, Federal Republic of

Reissmann, Thomas, Frankfurt, Germany, Federal Republic of
 Losse, Gunter, Dresden, Germany, Federal Republic of
 Naumann, Wolfgang, Zug, Germany, Federal Republic of
 Murgas, Sandra, Dresden, Germany, Federal Republic of
 PA Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of
 (non-U.S. corporation)
 PI US 6022860 20000208 <--
 AI US 1998-48244 19980326 (9) <--
 PRAI DE 1997-19712718 19970326 <--
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Moezie, F. T.
 LREP Pillsbury Madison & Sutro LLP
 CLMN Number of Claims: 7
 ECL Exemplary Claim: 1
 DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
 LN.CNT 271

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In this invention, a release-delaying system is to be developed for LHRH antagonists, in particular for cetrorelix, which allows the active compound to be released in a controlled manner over several weeks by complexation with suitable biophilic carriers.

The acidic polyamino acids polyglutamic acid and polyaspartic acid were selected for complexation with cetrorelix. The cetrorelix polyamino acid complexes are prepared from aqueous solutions by combination of the solutions and precipitation of the complexes, which are subsequently centrifuged off and dried over P.sub.2 O.sub.5 in vacuo. If complexes having a defined composition are to be obtained, lyophilization proves to be a suitable method. The cetrorelix-carboxylic acid complexes were also prepared from the aqueous solutions.

In the random liberation system, the acidic polyamino acids poly-Glu and poly-Asp showed good release-delaying properties as a function of the hydrophobicity and the molecular mass of the polyamino acid.

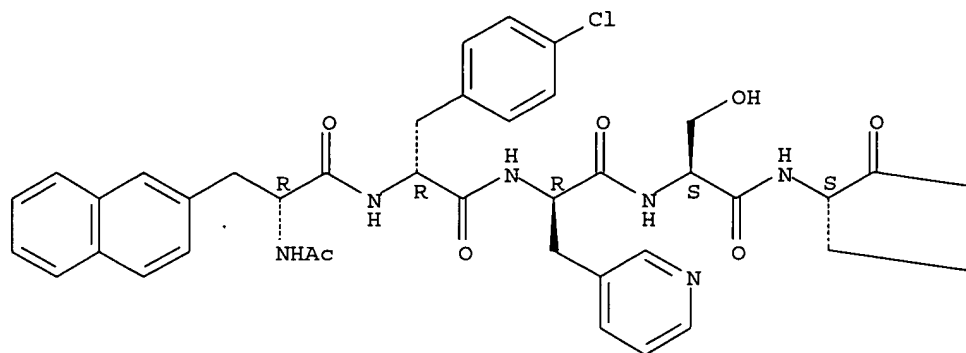
In animal experiments, it was possible to confirm the activity of the cetrorelix-polyamino acid complexes as a depot system in principle. It is thus possible by complexation of cetrorelix with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of active compound here can be controlled by the nature and the molecular mass of the polymers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

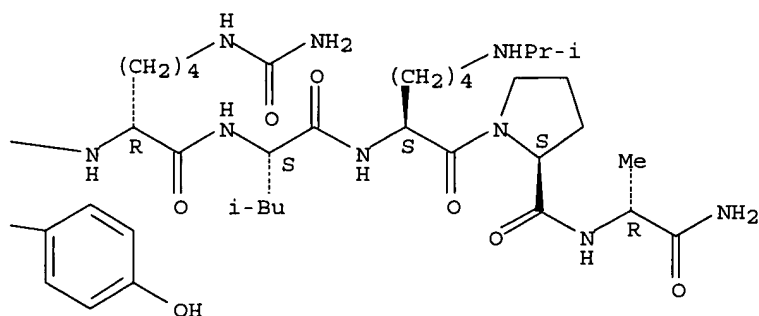
IT 151272-78-5D, Antarelix, complexes with poly(amino acids)
 (immobilized activity-stabilized LHRH antagonist complexes and their production)
 IT 151272-78-5D, Antarelix, complexes with poly(amino acids)
 (immobilized activity-stabilized LHRH antagonist complexes and their production)
 RN 151272-78-5 USPATFULL
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-(aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 21 OF 23 USPTAFULL on STN

AN 1998:150904 USPTAFULL

TI LHRH antagonist peptides

IN Roeske, Roger W., Indianapolis, IN, United States

PA Advanced Research & Technology Institute, Bloomington, IN, United States
(U.S. corporation)

PI US 5843901 19981201 <--

AI US 1995-480494 19950607 (8) <--

DT Utility

FS Granted

EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Borin, Michael

LREP Lahive & Cockfield LLP, DeConti, Jr., Giulio A., Kara, Catherine J.

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1660

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel LHRH antagonist peptides, pharmaceutical compositions thereof, and
methods of use thereof, are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186836-91-9P

(LHRH antagonist synthetic peptide analogs with pharmaceutical
applications as cancer inhibitors or contraceptive agents)

IT 186836-91-9P

(LHRH antagonist synthetic peptide analogs with pharmaceutical

applications as cancer inhibitors or contraceptive agents)

RN 186836-91-9 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-acetyl-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, mono(trifluoroacetate) (salt) (9CI)
(CA INDEX NAME)

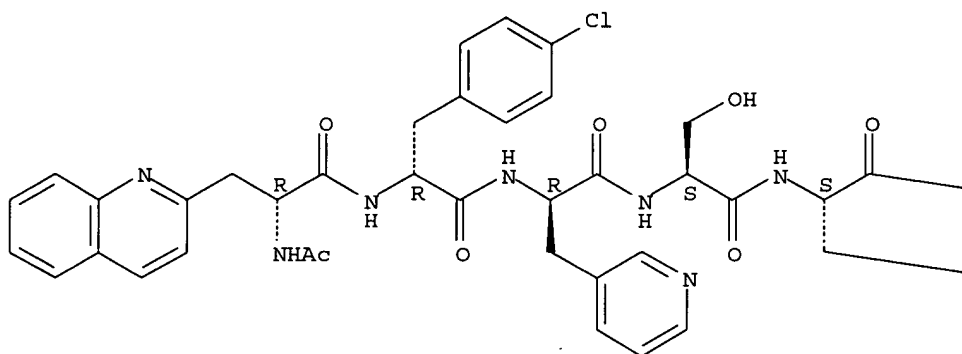
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CRN 186836-90-8

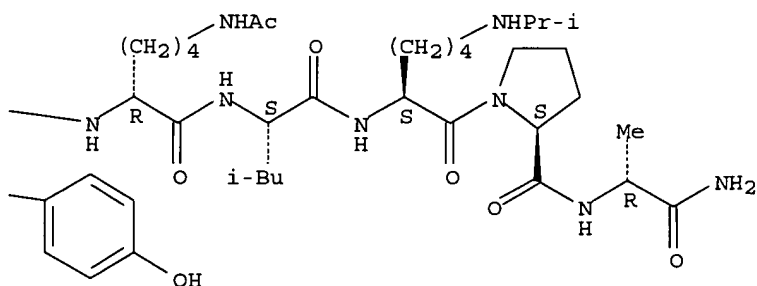
CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A



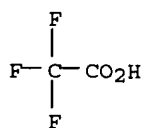
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



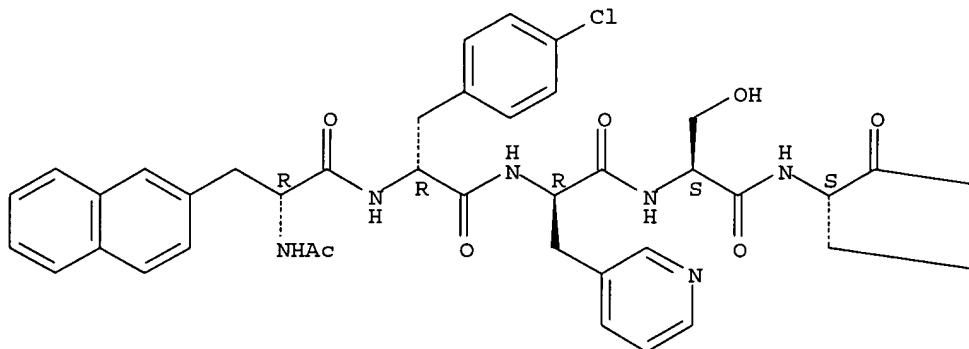
L24 ANSWER 22 OF 23 USPATFULL on STN
 AN 1998:75185 USPATFULL
 TI Long-acting injection suspensions and a process for their preparation
 IN Engel, Jurgen, Alzenau, Germany, Federal Republic of
 Klokkeers-Bethke, Karin, Lenggries, Germany, Federal Republic of
 Reissman, Thomas, Frankfurt, Germany, Federal Republic of
 Hilgard, Peter, Frankfurt, Germany, Federal Republic of
 PA Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of
 (non-U.S. corporation)
 PI US 5773032 19980630 <--
 AI US 1996-661017 19960610 (8) <--
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Azpuru, Carlos A.
 LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
 CLMN Number of Claims: 8
 ECL Exemplary Claim: 1
 DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
 LN.CNT 373
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Poorly soluble salts of LHRH analogues, for example cetorelix embonate,
 display an intrinsic sustained release effect in the grain size 5 µm
 to 200 µm.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

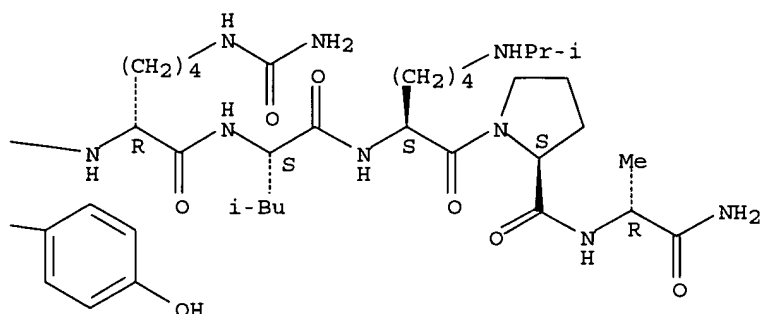
IT 151272-78-5, Antarelix
 (long-acting injection suspensions of poorly soluble LHRH analogs)
 IT 151272-78-5, Antarelix
 (long-acting injection suspensions of poorly soluble LHRH analogs)
 RN 151272-78-5 USPATFULL
 CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-
 phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-
 (aminocarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 23 OF 23 USPAT2 on STN

AN 2002:181669 USPAT2

TI LHRH ANTAGONIST PEPTIDES

IN ROESKE, ROGER W., INDIANAPOLIS, IN, UNITED STATES

PI US 2002115615 A1 20020822

AI US 1998-973378 A1 19980406 (8)

RLI Continuation of Ser. No. US 1995-480494, filed on 7 Jun 1995, PATENTED A 371 of International Ser. No. WO 1996-US9852, filed on 7 Jun 1996, UNKNOWN

DT Utility

FS APPLICATION

LREP CATHERINE J KARA, LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109

CLMN Number of Claims: 47

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 909

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a method for essentially complete oxidation of a concentrated liquor containing oxidizable organic matter. Each step of the method is performed under substantially superatmospheric pressure. Initially, the liquor is preheated to a temperature higher than about 10° C. below the boiling point of water at the substantially superatmospheric pressure. A feed formed of the concentrated liquor is then essentially completely oxidized at a temperature of at least 800° C. in the presence of a gas comprising at least sixty percent by volume of oxygen to form a suspension of a hot gas and a molten slag. The molten slag is separated from the hot gas before the slag is dissolved in water to form a brine. The separated hot gas is then cooled to a temperature below 250° C. by quenching with an aqueous liquid. Finally, the aqueous liquid is separated from the hot gas.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186836-91-9P

(LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)

IT 186836-91-9P

(LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)

RN 186836-91-9 USPAT2

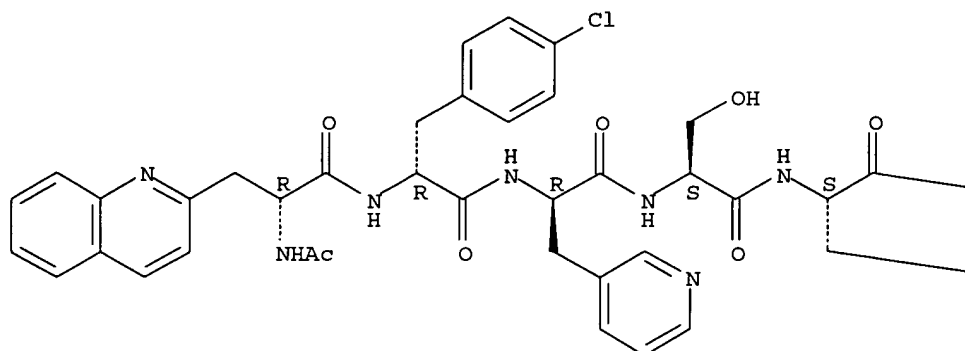
CN D-Alaninamide, N-acetyl-3-(2-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-acetyl-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, mono(trifluoroacetate) (salt) (9CI)
(CA INDEX NAME)

CM 1

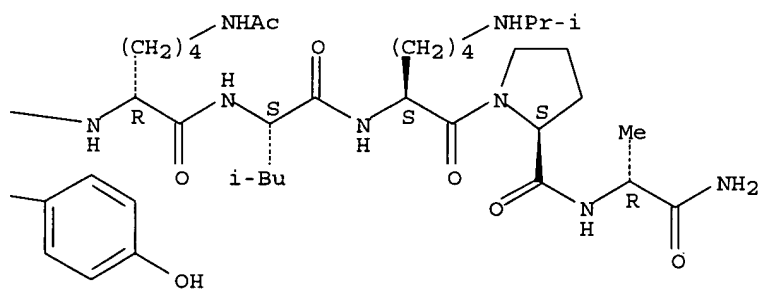
CRN 186836-90-8
 CMF C74 H100 Cl N15 O14

Absolute stereochemistry.

PAGE 1-A

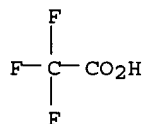


PAGE 1-B



CM 2

CRN 76-05-1
 CMF C2 H F3 O2



=> d his

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 ACT VANIK130F0/A

Noble Jarrell

21/11/2005

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      E DE GHENGI R/AU
      E BOUTIGNON F/AU
L8      20 E3-5
      E ZENTARIS/CS,PA
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      E ARDANA/CS,PA
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L20     3 E4
L21     33 (ZENTARIS OR ARDANA)/CS,PA
L22     8 L18 AND L19-21
L23     27 L18 NOT L22
L24     23 L23 AND L13
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